December 18, 2019 | contact: reports@seligman.com | previous reports: https://seekingalpha.com/author/seligman-investments

ALLAKOS (NASDAQ: ALLK)

A Suspect Biotech with a Phase 2 Farce, Incredulous Trial Investigators, and Warning Signs of Potential Fraud

$6.5B market cap | $132/share | $30/$140 52wk hi/low | $66M ADV, 30d avg | 8.5mm shares short/31% of float *as of 12/17/19**

Source: Bloomberg, all market data in report as of close 12/17/19

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

"My main reservation about the phase 2 data presentation…it's like when you get a letter in the mail that says you're inheriting $5 million from your long lost relative. It's amazing but it can't be right…One of the things about this company – they were the CRO for this trial. Which is interesting. They didn't use one. This doesn't normally happen. The company was actively involved during the trial. They were involved and aggressive. I don't want to go into subjective things. There were lots of circumstances."*

– Allakos ENIGMA Phase 2 Trial Investigator and prominent physician/key opinion leader (KOL) in the eosinophilic gastritis/esophagitis (EG/EoE) space, commenting on ALLK's publicly released trial results

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"Do eosinophils cause EG? Great question…EG and EoE symptoms are the trickiest thing. They're so heterogeneous and hard to measure. I was surprised that Allakos showed robust symptom change with such heterogeneous symptoms. It deserves some scrutiny."

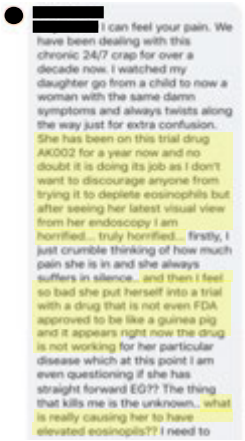
– Another ENIGMA trial investigator, one of six we spoke to, also a prominent KOL

"There's a lot of grandstanding. There's not a lot here. There's a lot of information that they're not showing. The data is odd and doesn't give you confidence…It looks to me like they manipulated these numbers to look good…The data is cherry-picked and dishonest…There are consistent problems throughout the presentation. It's sketchy. You couldn't do this for a clinical publication. This would not be publishable because you can't draw conclusions from it."

– PhD/scientist we engaged to analyze Allakos' trial data, who previously conducted due diligence at one of the largest biotech companies

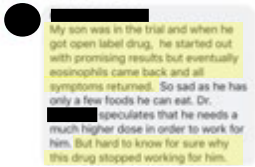
*Source: Seligman expert consultations / *Contract research organization*

Seligman Investments | ALLAKOS (NASDAQ: ALLK)



"[My daughter] has been on this trial drug AK002 for a year now and no doubt it is doing its job as I don't want to discourage anyone from it to deplete eosinophils but after seeing her latest visual view from her endoscopy I am horrified…truly horrified […] and then I feel so bad she put herself into a trial with a drug that is not even FDA approved to be like a guinea pig and it appears right now the drug is not working [...] what is really causing her to have elevated eosinophils??"

– October 21, 2019 post by parent of a patient who completed the Allakos Phase 2 ENIGMA trial in EG/EoE as well as the open label extension study. ENIGMA topline results were released on August 5, 2019. The extension study is ongoing but some participants or their families have publicly shared their results on Facebook. We wonder why Allakos withheld P2 endoscopy outcomes, as ENIGMA investigators and patient posts indicate the data was collected.



"My son was in the trial and when he got open label drug, he started out with promising results but eventually eosinophils came back and all symptoms returned […] hard to know for sure why the drug stopped working for him."

– October 21, 2019 post by another parent of a patient in the ENIGMA trial. The patient also "finished the open label trial" and "got the highest dose," per a follow up post.

"I haven't seen anything like this before. Scientifically they are relatively weak. There's been no chatter in our field about their trial results. No one follows this company. There are not a lot of research scientists involved…No one's sent me any emails, no questions. Since their results came out, there's been no discussion. No one's talked about it. Normally patients even go nuts and send me emails…I am skeptical. I personally don't know how this could be worth billions. It's crazy."

– Allakos ENIGMA Phase 2 Trial Investigator and prominent KOL in the EG/EoE space

Source: Facebook posts, "Eosinophilic Gastritis Support Group" https://www.facebook.com/groups/258285487951166/; Seligman expert consultations

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Executive summary

	Pages
Introduction to Allakos	*8-22*
22 WARNING SIGNS FOR INVESTORS:	
1. ***The failure of AK001, the precursor to Allakos' lead AK002 program and the canary in the coal mine**. AK001/AK002 are virtually identical Siglec-8 antibodies. The company has buried the results for the two AK001 studies it conducted, but our research indicates a debacle - followed by its lead pre-ipo investor dumping its entire stake at $2.48/share in August 2017; the company valuing itself at 93 cents/share weeks later, suggesting a valuation range of $31-83MM; cash dwindling to two months, requiring a bailout by remaining investors; and a new CEO, COO, CFO, CMO, and VP Clinical Ops. Yet a mere 11 months after this chaos, ALLK was re-packaged around "AK002" and a new, questionable phase 1 study in *healthy* volunteers and taken public – a benchmark feat of Wall Street hocus-pocus.***	*23-33*
2. ***Allakos has a checkered history of conducting small, low-credibility trials, marked by a striking level of what we consider to be discrepancies, omissions, cherry-picking, and other red flags.***	*34-46*
3. ***The company appears to have conducted the ENIGMA phase 2 EG/EGE trial itself and served as its "own CRO," with at least four different trial investigators expressing concerns around the company's conduct and the trial's integrity and compliance, describing it as "aggressive," "stupid," "dishonest," or as something that "won't fly with the FDA," and their own reactions as "shocked" and "very bothered." Based on investigators' concerns, we conducted further due diligence on whether biopsies were sent to the company itself or a panel of independent, third-party pathologists – and are troubled by what we found.***	*47-55*
4. ***Flagrant nepotism in key clinical roles, filled by the Chief Medical Officer's son and daughter. The daughter's profile states "class of 2012" in college. The children received options for 100k shares, worth ~$13MM at $130/share. We question why a public company didn't pick more qualified executives for its core function, and note the unusual geographic location of all three family members relative to Allakos' only listed office.***	*56-61*
5. ***Poor controls as well as Allakos' role in running the study itself rendered the ENIGMA trial – purportedly randomized and double-blind - essentially unblinded, making the already subjective endpoint of patient-reported symptom scores a sham. The FDA has cautioned that "Suspicion of inadvertent unblinding can be a problematic review consideration for the FDA when assessing PRO endpoints." Shockingly, a parent posted about speaking to Allakos - the co-founder plus what we infer to be contact with the CMO - which if true would strike us as reckless and raise concerns about trial tampering and Allakos' conduct in general.***	*62-77*

Executive summary (cont'd)

Pages

6. ***What appears to be a last minute, unexplained expansion of the ENIGMA trial, with insufficient time for new patients to complete the study's pre-specified protocol, then followed by the exclusion of patients for a cherry-picked "Per Protocol" group around which the topline results are framed – a curious scenario given Allakos' role in running the study, nepotism, unblinding – and as we detail later, the role of one or two patients in barely pushing the study into statistical significance, despite n=65, according to a number of biostatisticians we consulted, including two known for identifying discrepancies or fraud in clinical trials.*** *78-86*

7. ***The ENIGMA trial allowed steroid use in a liberal, widespread manner, rendering the results utterly flawed and compromised as steroids are the standard of care for EG/EGE and rapidly reduce eosinophil levels and symptoms. Biostatisticians, trial design experts, and ENIGMA trial investigators echoed concerns of steroids as a confounding factor. Absurdly, greater than 10mg of Prednisone use was an exclusion criteria, yet doctors pre-dosed patients with an amount 8X or higher prior to infusion of AK002.*** *87-107*

8. ***The August 5th ENIGMA topline results provide a master class in fatal discrepancies and internal contradictions. The red flags are so numerous that we consider the presentation to be little more than sleight of hand. We have never seen the sheer number of warning signs in a single trial's results as we do here.*** *108-115*

9. ***Aside from discrepancies, the trial results are compromised by 1) glaring omissions, 2) cherry-picked measures, and 3) statistical gimmicks and obfuscation, making a mockery of standard biotech disclosure and indicative of a trial where all is not as it appears.*** *116-121*

10. ***Since the superficial ENIGMA release on Aug 5th, Allakos has yet to follow up with proper data at a medical conference or in a peer-reviewed publication, which we find alarming relative to standard practice. The company has had three key opportunities to fill in gaping holes and failed to do so. The scraps of additional data which have been shared raise more questions than answers, with red flags beyond those in the Aug 5th package. Alarmingly, critical information from Aug 5th – such as p-values – keeps shifting, suggesting a lack of data integrity, incompetence, or worse. Further, the Aug 5th presentation appears to have now been deleted from the Allakos site, replaced by one less than half the length and missing key data in the original.*** *122-129*

11. ***Aside from shifting and instable p-values, the incremental data shared since Aug 5th is troubling for other reasons. The only real attempt at filling in gaps is a new slide with PRO response rates over time. However, the curves demonstrate that the response rates are flimsy and clinically irrelevant, strain credibility on other counts, and expose new discrepancies and contradictions that further undermine the ENIGMA results and cast doubt on the company's conduct.*** *130-140*

Executive summary (cont'd)

Pages

12. ***Allakos' representation of only one drug-related serious adverse event in the ENIGMA trial conflicts with numerous Facebook posts by trial participants** or their families. If a company misreports one critical piece of data, we wonder what else may be misreported: there is rarely just one cockroach. We are concerned that Allakos raised ~$400MM days after the ENIGMA results with disclosure that appears to be flatly contradicted by patients.* — *141-145*

13. ***Allakos reported a lack of vomiting at baseline and end of treatment in the ENIGMA trial and omitted "vomiting" in the list of adverse events - representations which are wildly inconsistent with patient accounts on Facebook.** Trial investigators were incredulous at Allakos' claim, raising worrying questions for investors given that vomiting is one of the most prevalent symptoms in the EGID patient population.* — *146-151*

14. ***Unclear and shifting trial timelines, in apparent violation of the pre-specified protocol, suggestive of cherry-picking timeframes to engineer favorable results**. The pre-specified protocol was already concerning given that tissue eosinophil and PRO endpoints were to be measured at different intervals. Given the numerous red flags around Allakos' conduct and the trial's integrity, we find the lack of clarity worrisome – and wonder if cutting the data at the original interval would have led to trial failure.* — *152-155*

15. ***The ENIGMA trial used a fatally flawed PRO questionnaire whereby patients self-assessed their symptoms**. Demonstrating symptom improvement is necessary per recent FDA guidance for EGID trials. The use of a reliable, validated PRO questionnaire is a pivotal determinant of how the FDA will evaluate Allakos' results, and Allakos' PRO was neither.* — *156-162*

16. ***Significant trial design problems beyond a faulty PRO. The ENIGMA endpoints were superficial relative to competing EGID trials and FDA guidance**, which incorporate a more robust battery of symptom, histologic, and endoscopic measures, even in phase 2. **In particular, Allakos' failure to disclose endoscopy data – which trial investigators told us was collected – is worrisome**. Papers by even ENIGMA investigators attest to the accuracy of endoscopic scoring.* — *163-165*

17. ***The ENIGMA trial design lacks credibility and relevance for other reasons, which we expect to haunt the company in phase 3**. The trial enrolled patients 18 and above, an odd choice given the prevalence of EG/EoE in patients <18 and recent FDA guidance on the importance of including adolescents in EGID trials. Trial investigators expressed incredulity at other aspects of the cohort selected, stating that it was atypical and marked by discrepancies. We get the sense that Allakos went out of its way to cherry-pick an unrepresentative population, and given that ALLK ran the study itself, we wonder if it was even randomized.* — *166-170*

Executive summary (cont'd)

Pages

18. ***The mystery of the missing blood eosinophil data**. Allakos has touted AK002's powers in reducing blood eosinophils, but has withheld data ever since a phase 1 in healthy volunteers – remarkable silence given that subsequent AK002 trials have included it as an endpoint, not to mention it being a standard feature of competing trials. The ENIGMA trial disclosed baseline blood eosinophil levels, but shared ending ones only for tissue. Blood eosinophils are easily measured in CBC panels, while tissue biopsies are vulnerable to bias, irregular cell distribution, cherry-picking – and the pathologist's conflicts of interest. We detail uncomfortable questions lurking behind Allakos' strident assertions of AK002's inhibitory abilities.* *171-180*

19. ***The mystery of the missing mast cell data.** The Allakos story hinges on AK002's ability to remove both eosinophils and mast cells, as both express Siglec-8. Either Siglec-8 inhibition works or it doesn't. Company materials suggest that mast cells are the driver of eosinophil "activation and recruitment." Yet given the centrality of mast cells to the story, the company's reluctance to share basic data mirrors the lack of disclosure on blood eosinophils. The scraps of data shared are troubling, and notably omit tryptase levels – the only relevant measure of mast cell activity. One of the world's top mast cell research scientists dismissed the Aug 5th ENIGMA mast cell claims as "not significant, relevant, or clinical effects."* *181-192*

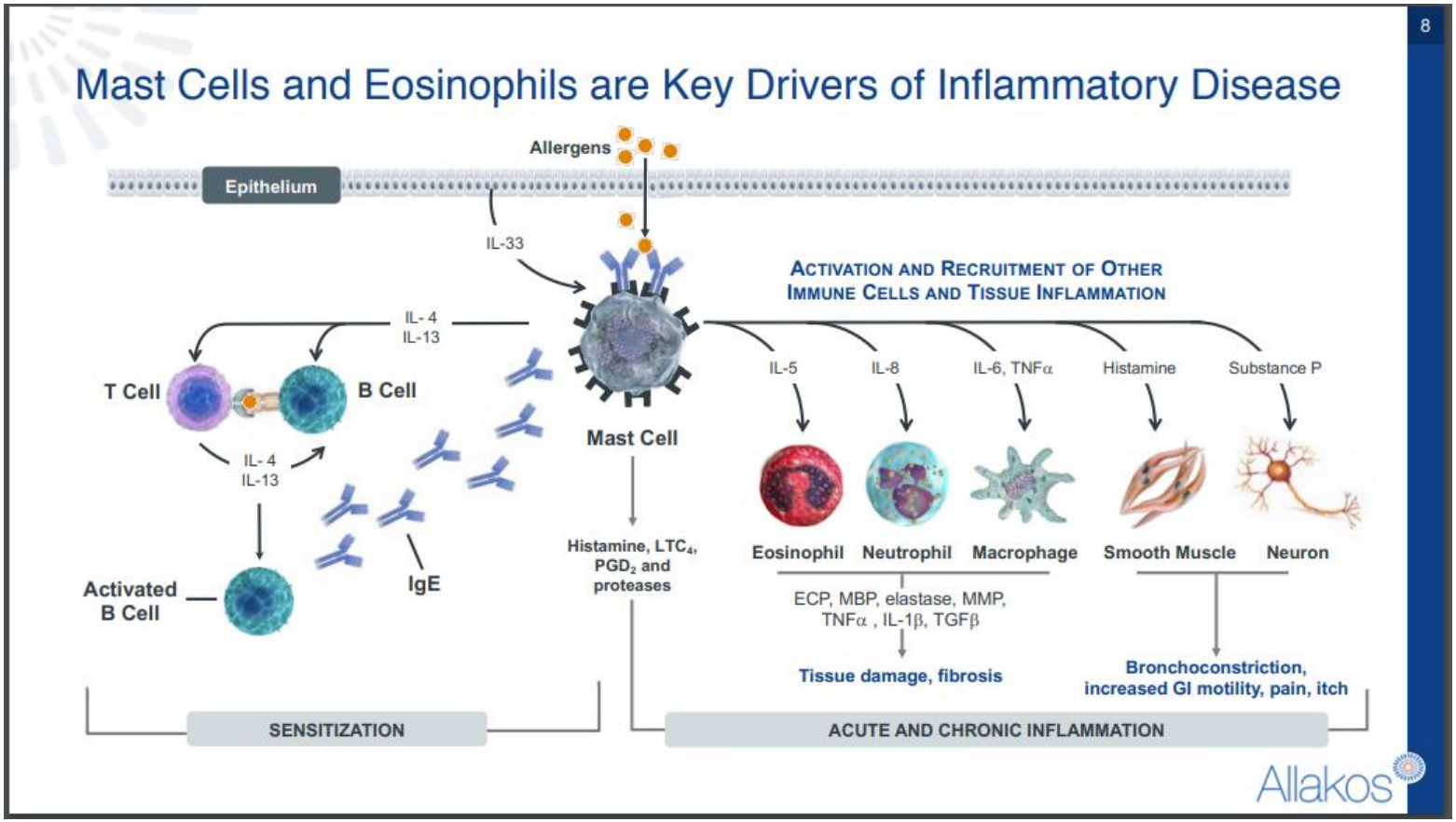
20. ***The ENIGMA tissue eosinophil reductions are suspiciously higher than shown in previous AK002 data from cell culture experiments and animal models**. Allakos claims 97% reduction in tissue eosinophils, yet is reluctant to share blood eosinophil counts. In our opinion, the ENIGMA eosinophil reductions are simply too good to be true and fail the smell test – a sentiment shared by trial investigators.* *193-197*

21. ***Even if one assumes AK002 isn't a P3 flop, it's commercial future is bleak as a me-too late-mover drug in a crowded space.** Investigators stated that 6-8 hour infusions, monthly for life, render it dead-on-arrival. A realistic EG/EoE TAM implies at most $100-200MM in AK002 US sales. Influential ENIGMA investigators were devastating in stating that AZN's benralizumab and REGN's dupilumab are far ahead, and pointed to a long list of competing EoE/EG trials that ALLK investors appear unaware of. We encourage investors to study recent P2 data for dupilumab (Oct 2019) and benralizumab (Apr 2019) – stronger than AK002's ENIGMA results - and to watch for upcoming data from competing trials.* *198-209*

22. ***Allakos appears to have a pattern of not playing by the rules, beyond those pertaining to trials**. In addition to making a mockery of biotech disclosure practices, compliance, and data integrity, we note 1) the suspicious timing of a recent option grant, which raises concerns of backdating and "spring-loading"; 2) apparent violation of rules for papers at medical conferences; and 3) questionable behavior with regard to Reg FD.* *210-215*

Introduction to Allakos

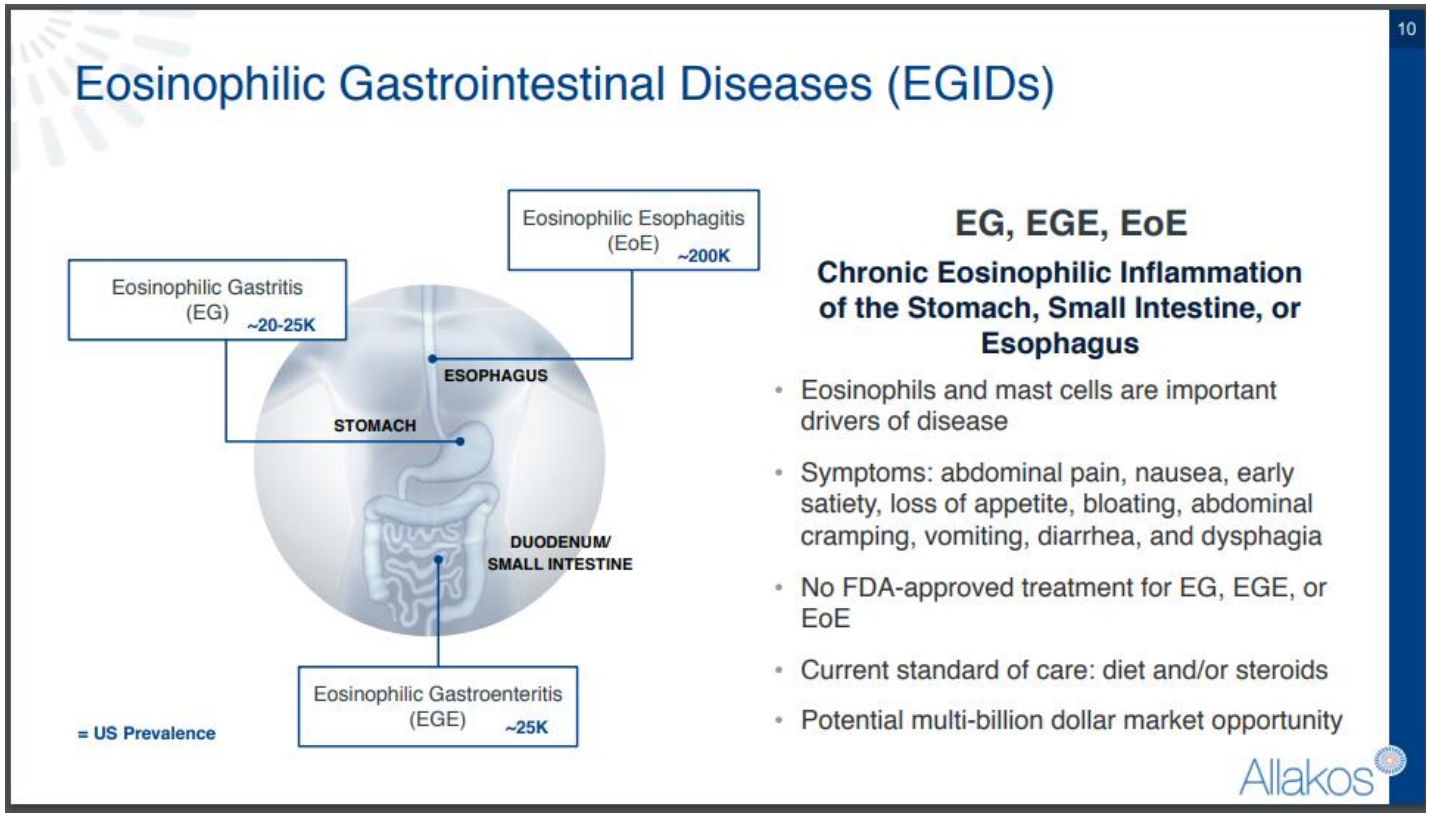
Allakos is an early-stage, one-drug biotech company with a ~$6.5B market cap based on the recent results of a phase 2 trial with 65 patients. Its sole program is AK002, also known as antolimab, a monoclonal antibody that targets the Siglec-8 receptor on eosinophils and mast cell, two types of white blood cells that play a role in immune and inflammatory response. The company is predicated on two assumptions: 1) elevated numbers of eosinophils and mast cells drive certain conditions and their symptoms, and 2) by purportedly reducing these cell counts, AK002 leads to symptom improvement.



Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm

Introduction to Allakos

Allakos feels that eosinophils and mast cells play a role in many diseases, but is mainly focused on eosinophilic gastrointestinal diseases (EGID's). The lead indication for AK002 comprises eosinophilic gastritis (EG) and eosinophilic gastroenteritis (EGE). On August 5th, the company announced top-line results for its Phase 2 ENIGMA trial in EG/EGE, with teaser data provided for eosinophilic esophagitis (EoE), for which it expects to conduct a separate trial. The company is currently conducting an open-label extension study in EG/EGE, which appears to be its only active trial. Allakos hopes to start a phase 3 in EG/EGE and phase 2/3 in EoE, both in 2020 – all with AK002, its sole program.



Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

The August 5th ENIGMA results stated the trial met its endpoints of tissue eosinophil and symptom reduction. Despite being a mere phase 2 trial with n=65, the stock doubled within a day and nearly tripled in a week. The company provided only superficial top-line data, marked by an extraordinary number of what we believe to be discrepancies, omissions, cherry-picked statistics, and other red flags that we detail in this article. Nonetheless, the company pulled off an astonishing ~$400MM secondary within days of the release. Raising such a large amount strikes us as bold and reckless, given the escalated legal stakes if certain ENIGMA trial representations made on August 5th – such as endpoint p-values, adverse effects, prevalence of key symptoms - were ever proven to be false or fraudulent.

Source: Bloomberg stock chart

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

A screen of all public biotech companies worldwide suggests that at ~$6.5B market cap, Allakos is not only the most expensive pre-revenue biotech on the planet, but appears to be the most expensive globally based on just phase 2 data, and the 32nd most richly valued overall. With n=65 in its ENIGMA trial, investors are valuing the company at $100MM per phase 2 patient data point. If Allakos were an oncology, gene therapy, and CBD company rolled into one we could perhaps understand investors' high expectations.

Company Name	Market cap	LTM revenue
Amgen Inc. (NasdaqGS:AMGN)	144,292	23,395
AbbVie Inc. (NYSE:ABBV)	132,251	32,867
CSL Limited (ASX:CSL)	88,505	8,539
Gilead Sciences, Inc. (NasdaqGS:GILD)	83,753	22,365
Vertex Pharmaceuticals Incorporated (NasdaqGS:VRTX)	56,444	3,620
Biogen Inc. (NasdaqGS:BIIB)	53,611	14,233
Regeneron Pharmaceuticals, Inc. (NasdaqGS:REGN)	40,351	7,622
Alexion Pharmaceuticals, Inc. (NasdaqGS:ALXN)	24,302	4,736
Grifols, S.A. (BME:GRF)	20,942	5,409
Incyte Corporation (NasdaqGS:INCY)	19,668	2,108
Celltrion, Inc. (KOSE:A068270)	19,661	825
Seattle Genetics, Inc. (NasdaqGS:SGEN)	19,403	801
BioMarin Pharmaceutical Inc. (NasdaqGS:BMRN)	14,977	1,603
Genmab A/S (CPSE:GMAB)	14,476	532
Galapagos NV (ENXTAM:GLPG)	13,758	943
Exact Sciences Corporation (NasdaqCM:EXAS)	13,464	724
Alnylam Pharmaceuticals, Inc. (NasdaqGS:ALNY)	12,994	169
Chongqing Zhifei Biological Products Co.,Ltd. (SZSE:300122)	11,216	1,315
Sarepta Therapeutics, Inc. (NasdaqGS:SRPT)	10,089	365
Neurocrine Biosciences, Inc. (NasdaqGS:NBIX)	9,992	676
BeiGene, Ltd. (NasdaqGS:BGNE)	9,957	430
Ionis Pharmaceuticals, Inc. (NasdaqGS:IONS)	8,993	821
BioNTech SE (NasdaqGS:BNTX)	8,609	157
Shenzhen Kangtai Biological Products Co., Ltd. (SZSE:300601)	8,322	267
Amarin Corporation plc (NasdaqGM:AMRN)	7,659	364
ACADIA Pharmaceuticals Inc. (NasdaqGS:ACAD)	7,104	300
argenx SE (ENXTBR:ARGX)	6,983	72
Walvax Biotechnology Co., Ltd. (SZSE:300142)	6,913	154
Hualan Biological Engineering Inc. (SZSE:002007)	6,820	534
The Medicines Company (NasdaqGS:MDCO)	6,740	-
Arrowhead Pharmaceuticals, Inc. (NasdaqGS:ARWR)	6,605	169
Allakos Inc. (NasdaqGS:ALLK)	**6,450**	**-**

**MDCO LTM $0, historically >$650MM/year*

Source: CapitalIQ screen of all public biotech companies globally, as of 12/17/2019

Introduction to Allakos

As we dug into Allakos, we took note of its curious history and dramatic ascent from near-death just two years ago. After the failure of its AK001 Siglec-8 antibody in 2017, its lead pre-IPO investor indicated it would not invest any more cash and dumped its entire stake at $2.48/share, in Aug 2017; we believe this firm's principal was ALLK's then-Chairman; the company nearly ran out of cash; and the remaining venture capital-led board flushed the management team. In a pre-IPO letter to the SEC, Allakos' lawyers – who requested "FOIA confidential treatment" – described turbulent internal dynamics and revealed that at the time of this shift to AK002 in 2017, the company "had no lead indication identified." The company did a bridge financing with remaining investors, presumably near the 93 cents/share the company valued itself a few weeks after the lead investor fled. Whether one uses $0.93 or $2.48, our math suggests that those who knew Allakos best valued it between $31-83MM as recently as ~2 years ago in Aug 2017.

*"In connection with the management team transition, the Company reevaluated its lead product candidate at the time, AK001. **In June 2017**, due to the greater activity of the Company's other product candidate, AK002, as compared to AK001, the Company decided to focus its development efforts on AK002 and discontinued the development of AK001. **At this time, as a result of the shift to AK002, the Company had no lead indication identified."***

*"During this time frame the Company's cash resources continued to dwindle, which constrained its activities and limited its plans. **At one point, in August 2017, the Company's cash resources were sufficient only to support two more months of operations and required the Company to conduct a bridge financing with its existing investors."***

"August 31, 2017 Valuation…The resulting estimated fair value of the Company's common stock was $0.93 per share…"

Source: SEC correspondence https://sec.report/Document/0001193125-18-200129/; ALLK S-1 indicated 33.5MM shares (33.5MM x $0.93=$31MM, 33.5MM x $2.48 = $83MM), https://www.sec.gov/Archives/edgar/data/1564824/000119312518219134/d447521ds1a.htm

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

A pair of venture capital firms owned more than half the stock, and installed their colleagues of 7+ years as CEO and COO, along with a new CFO, CMO, and VP Clinical Operations. The haste with which the new regime took Allakos from "zero to hero" is remarkable. With the story quickly repackaged around a "new" hasn't-failed Siglec-8 antibody – supported by the requisite phase 1 study in healthy volunteers and "promising preclinical animal data in December 2017 in a mouse model of the lead indication of EG/EGE"[1] – the company raised a Series B financing at $7.93/share ($266MM valuation, by our math), and managed to go public in July 2018 with a day-one close of $35, all within a year of not even having a lead indication. Perhaps parachuting in two former vc's from the firm with the largest stake at IPO is all it takes for an instant scientific and clinical turnaround, or perhaps investors would be wise to exercise caution. To understand which scenario was more likely, we spoke with an ENIGMA trial investigator, a prominent physician and KOL. We characterize the level of incredulity as off the charts:

> *"My main reservation about the published phase 2 data…it's like when you get a letter in the mail that says you're inheriting $5 million from your long lost relative.* ***It's amazing but it can't be right****. In typical data, you never see data like this.* ***It's unheard of*** *to see data this strong. I do a lot of research and* ***even in a mice system you don't see this*** *type of data. It's just remarkable. In some ways* ***it's too good to believe. I'm an expert in the area and one of the leaders****. We typically don't see this.* ***Sometimes, something is too good to be believe. Sometimes, you know, I say wow, I'd like to see this reproduced. I'm concerned*** *at how striking the data is.* ***I just have this concern - how could they have data like this?"***
>
> ***– Allakos ENIGMA Phase 2 Trial Investigator and an influential physician/KOL in the eosinophilic gastritis/esophagitis space, commenting on the company's publicly released trial results***

Source: [1] https://sec.report/Document/0001193125-18-200129 ; Bloomberg; Seligman expert consultations; ALLK press releases

Introduction to Allakos

We expanded our investigation to include consultations with six ENIGMA trial investigators, who we estimate enrolled at least half of the patients in the trial. We also spoke with or engaged on a project basis: three experts in statistical analysis of clinical trials, including two known for identifying discrepancies or fraud, as well as four scientists and researchers. All discussions were restricted to publicly published trial results and conducted in accordance with best-practice research/compliance guidelines, including monitoring of calls as deemed necessary.

Six ENIGMA trial investigators.
- We asked each to carefully study and opine upon the ENIGMA topline results publicly released on Aug 5th
- Three are prominent physicians/KOL's in the EGID space
- Our calls suggest an interesting divergence between multiple investigators' actual opinions and what they may be asked or willing to say in potential broker or company-sponsored commentary

Three experts in statistical analysis of clinical trails
- Two professors of mathematics/statistics/biostatistics
- Two are known for identifying discrepancies or fraud in trials
- All are extensively published with decades of experience

Four scientists and researchers, including one of the most prominent worldwide in Allakos' space
- All have extensive expertise in trial design and analysis
- One conducted scientific due diligence at one of the largest biotech companies

Two other experts
- A scientist/former employee of Allakos
- An expert in biotech due diligence

An intensive review of the clinical literature, public filings, transcripts, and press releases

All former employees were at least six-months removed from the company, per best practice research and compliance guidelines. All experts agreed to not provide any information which is inconsistent with any non-disclosure, confidentiality, or other agreements or understandings. We mask their names to respect their privacy.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

We took note of other indicia, which we have historically associated with frauds and promotes and found helpful in discriminating "real" vs. "vaporous" biotech companies. We make no allegation that Allakos is a fraud, and emphasize that our inference of any such indicia or warning signs is strictly our opinion based on our research, which we encourage readers to independently verify.

1. Unusual fixation on short sellers

- At a group meeting, we asked the CEO a clarification question about steroid use as a confounding factor in the ENIGMA trial. He erupted into a riff on short-sellers and taunted people to "short our stock."
- At its February 2019 investor day, Allakos allegedly refused entry to an analyst with a sell rating
- At a small but influential November 2019 EGID conference in Cincinnati, Allakos employees were observed to be aggressively trying to interfere with investor conversations with KOL's, per an eyewitness account.

2. Paranoia about investor scrutiny and basic Q&A

- ALLK does not hold quarterly earnings calls, much less announce earnings dates, an anomaly with a high hit rate in predicting biotech blow up or fraud, in our experience.
- Amazingly, Allakos failed to announce the Oct 22nd ENIGMA presentation at UEG in Barcelona, its first opportunity since the Aug 5th topline results to disclose more than superficial information. Companies with positive trial data usually promote and seek out investor attention at marquee medical conferences.
- We consider the lack of UEG notification, slides, or an 8-K filing to be a very likely Reg FD violation. The sell-side appears to have been in the dark, as well.
- August 5th ENIGMA presentation appears to have now been deleted from the Allakos IR site

3. A remarkable lack of clinical publications, much less validation or interest from the KOL community

- The Allakos website and clinical literature are a barren desert beyond a few meaningless AK002 posters
- Credible biotech's have a long list of publications by KOL's staking their reputations on serious science.
- Difficult to find anything on Siglec-8 not published by the co-founder of Allakos and a tiny inner circle, which we find unusual for a mechanism with the purported significance of AK002.

Source: Seligman meetings, expert consultations, and other research and analysis; ALLK website, press releases, and SEC filings

Introduction to Allakos

4. An aversion to peer-review by a credible medical journal
- ─ Alarmingly, the company has still not published proper ENIGMA data in a peer-reviewed medical journal, nor for any prior AK001 or AK002 trials we can locate
- ─ The superficial information shared to date would almost certainly be rejected for publication

5. Negligible historical R&D, and only asset licensed for almost nothing – reliable indicators of something amiss, as credible science/drugs/platforms require investment proportional to their potential
- ─ ALLK has a $6.5B market cap and a mere 42 employees in R&D per its last 10K, or $156MM per R&D head
- ─ S-1 states that AK001/AK002 were licensed in Dec 2013 with payments of $300K as of March 2018 and "may be required to make aggregate additional milestone payments of up to $4.0 million."
- ─ In 2016 and 2017, pivotal years for AK002 development, only $3MM and $5MM in AK002-related costs are disclosed, and only $15MM and $19MM of total R&D

6. A trivial number of employees relative to market cap, relatively brief operating history, and high executive turnover
- ─ LinkedIn employee count timeline shows 45 employees at time of IPO in July 2018
- ─ Only 79 employees currently per LinkedIn (as of 12/17/19), or $82MM market cap per employee

7. Sell-side information vacuum with infrequent, superficial coverage - unusual for a $6B market cap
- ─ Only four firms cover the stock: the three IPO underwriters plus a PR firm with a colorful history: *"LifeSci invited 70 female promotional models from prestigious modeling agencies…we made a serious mistake…"*[1]

Source: Bloomberg, CapitalIQ; ALLK SEC filings; Linkedin; [1] https://www.fiercebiotech.com/biotech/lifesci-advisors-aim-for-model-behavior-after-serious-mistake

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

We were further troubled by ALLK's pattern of releasing superficial trial data and dangling a proper presentation at "an upcoming medical conference" - only to not follow through. We asked the CEO a polite question in August about steroid use in the ENIGMA trial, and found his reaction surprising. He stated that he was tired of the question and blamed short sellers and their "intentional lies"; that the company has disclosed more data than anyone else; that the FDA was absolutely not concerned about steroids as a confounding factor (in contradiction to FDA EGID guidance, as we shall cover); that he asked investors if more data was necessary and they said no; that ALLK would publish more detailed data when he went to NYC in a few weeks; and that anyone who didn't believe him should "short our stock." No such data was published, and Allakos appeared to be a no-show a few weeks later at a key NYC healthcare conference.

Jan 7, 2019 press release on AK002 P2 results in subgroup of chronic spontaneous urticaria patients

"Top-line data are presented below; additional results from the study will be presented at an upcoming medical conference."

Source: http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-2-results-cohort-xolair-naive

Jan 29, 2019 press release on AK002 P2 results in two other urticaria cohorts

"Top-line data are presented below; more detailed results from the study will be presented at an upcoming medical conference."

Source: http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-2-results-patients-cholinergic

Feb 11, 2019 press release on AK002 P2 results in a fourth urticaria cohort

"Efficacy data from the Xolair failure cohort are presented below; more detailed results from the study will be presented at an upcoming medical conference."

Source: http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-2-results-ak002-patients-xolair

Feb 19, 2019 press release on AK002 P1 results in indolent systemic mastocytosis

"Data for the combined cohorts are presented below; ***more detailed results from the study will be presented at an upcoming medical conference."***

Source: http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-1-results-ak002-indolent

May 7, 2019 press release on AK002 P1 results in allergic conjunctivitis

"Data are presented below; ***more detailed results from the study will be presented during the conference call being held today and at an upcoming medical conference."***

Source: http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-1-results-ak002-indolent

Source: CEO comments from August 2019 broker-sponsored meeting. Comments are paraphrased from notes, not a precise transcript, subject to errors typical of such recollection, and may not be relied upon as an accurate rendition of statements made.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

Two weeks ago on Dec 4th, ALLK stock jumped 40% after Bloomberg indicated the company "is sounding out interest from potential buyers including global pharmaceutical and biotechnology companies." Although we are unaware of any early-stage biotech which has not been sounding out interest since the day it was founded, we found the timing of the leak curious – coming one day after a series of Form 4's disclosing massive RSU grants to the management team. The grants were made three business days prior, on the Friday after Thanksgiving for 312k RSU's, worth $43MM after the leak. Allakos has a pattern of suspect grant timing, including one we detail later which poses interesting legal questions for officers and directors (p.211). We found the leak questionable for another reason: the very same day, ALLK entered into a 10 year lease agreement with payments we estimate at ~$70MM. We wonder why a management team supposedly in active m&a discussions would commit to such a large, long-term deal.

Source: https://www.bloomberg.com/news/articles/2019-12-04/u-s-biotech-firm-allakos-said-to-weigh-options-including-sale; Bloomberg stock chart; ALLK Form 4's filed 12/3/19 https://www.sec.gov/cgi-bin/browse-edgar?action=getcompany&CIK=0001564824&type=&dateb=&owner=only&count=40; 8-k for new lease https://www.sec.gov/ix?doc=/Archives/edgar/data/1564824/000156459019045534/allk-8k_20191204.htm

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

The circumstances around the leak are curious for other reasons. The Bloomberg article stated the company is working with a "a financial advisor" according to "people who asked to not be identified." The same afternoon, Bloomberg published a second article framed on the thoughts of a 2015 college graduate and analyst at LifeSci Advisors, who rattled off a list of potential acquirers – the proverbial laundry list of large caps. The article failed to disclose LifeSci's relationship with ALLK, although a revision added that LifeSci provides investment banking services to ALLK and that funds managed by its affiliates have a "financial interest" in ALLK. We do not know whether LifeSci is the "financial advisor" in the Bloomberg leak, but in general find stock promotion via paid equity research more appropriate for questionable micro-caps and question why ALLK works with a firm of LifeSci's notoriety.

"More than 230 leaders of the biopharma industry have signed ***an open letter expressing outrage and calling for an end to the use of 'scantily clad' female models and dancers*** *at professional networking events. The letter was circulated…****in response to the LifeSci Advisors After Party…'where young, female models were brought in to escort the guests…****" -"Industry leaders take stand against sexism", Biocentury 2/4/2016*

"These stock promotion firms, in turn, hired writers to publish cheerleading articles that did not publicly disclose payments*….what is amazing and troubling about the SEC's enforcement action is the deep involvement and brazen misbehavior of biotech CEOs…* ***Here are some of the worst and most noteworthy offenders, culled from the SEC's complaints****…In the SEC complaint targeting Lidingo… NeoStem CEO Robin Smith hired Lidingo…* ***Most recently, Smith has was named co-chair of an advisory board on gender diversity in biotech formed by LifeSci Advisors…" – "For These Small-Cap Biotech CEOs, Stock Promotion, Not Drug Development, Was Priority No. 1", TheStreet.com 4/11/2017***

Source: https://www.bloomberg.com/news/articles/2019-12-04/u-s-biotech-firm-allakos-said-to-weigh-options-including-sale; https://blinks.bloomberg.com/news/stories/Q20CFRT0G1KX; LinkedIn profile of LifeSci analyst quoted in article https://www.linkedin.com/in/sam-slutsky-91113941/; https://www.allakos.com/news/press-release/121317/; https://www.biocentury.com/bc-extra/politics-policy/2016-02-04/industry-leaders-take-stand-against-sexism; https://www.thestreet.com/investing/stocks/for-these-small-cap-biotech-ceos-stock-promotion-not-drug-development-was-priority-no-1-14082476

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

Whichever potential suitors LifeSci has in mind for Allakos, we doubt Astra Zeneca will be one – nor others who observed its experience The CEO of Allakos previously ran ZS Pharma, which he sold to Astra Zeneca in 2015 for $2.7B (that is, less than half of ALLK's current valuation). The President/COO, Chief Medical Officer, and Chief Commercial Officer of Allakos are all ZS alumni. ZS was purportedly on the cusp of approval for its hyperkalemia drug at the time of sale, but instead the deal turned out to be a high-profile disaster for AZN. Bloomberg filed FOIA requests which conveyed a troubling compliance approach at ZS. A former M&A executive from a large pharma company, who we consulted for color on Allakos management, shared his experience buying a different company where the Allakos CEO was previously the lead venture capital investor: it "was dressed up," "none of the drugs worked," "I'd be more cautious" buying another drug from "that team."

"The $2.7bn takeout of ZS in 2015 looks like a bad misstep *now that ZS-9, the sole asset involved, has just received its second US complete response letter…****While the ongoing disaster of the ZS acquisition…" – Evaluate Group article, 3/17/17***

"When AstraZeneca PLC paid $2.7 billion for an experimental drugmaker in 2015, it had its sights set on a potential blockbuster medicine. ***Instead, it got a Texas factory riddled with defects and two scathing reviews from U.S. regulators rejecting the treatment…The facility run by ZS Pharma in Coppell, Texas, is at the heart of the Food and Drug Administration's objections****…The trouble began in March 2016 when an FDA inspection report cited a "reddish-brown substance" resembling rust in the tanks at the Texas facility. Reactors that were supposedly clean were found to be "soiled" with a white residue…When inspectors returned to the facility, they found a number of new issues including a worn-out, torn reactor gasket with pieces missing…Black particles were scattered on the face of the gasket,* ***and the plant's facilities weren't maintained to ensure the quality of products." – Bloomberg investigative article, 12/6/17***

"The company was dressed up, in retrospect*. Should we have raised alarm bells that other acquirers gave up, maybe. They had done a lot of work.* ***None of the drugs worked and the whole thing is dead****. It was not a smart deal for us.* ***If I was going to go back to that team to buy another drug, I'd be more cautious." – Former M&A executive a large pharmaceutical company***

Source: https://www.evaluate.com/vantage/articles/news/astras-mistakes-mount-0; https://www.bloomberg.com/news/articles/2017-12-06/frayed-gasket-delaying-astra-s-zs-9-shows-perils-of-pharma-m-a; Seligman expert consultations

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Introduction to Allakos

The leaks suggest that ALLK is loathe to enter phase 3 territory and is in a "hail-mary" phase with every incentive to kick up dust before scrutiny arrives in the form of FDA review. The fuse from P2 hype to reality is short. With no call since the Aug 5th ENIGMA results, the radio silence has been deafening. The Q3 release on Nov 12th was a few sentences with no next steps, no mention of peer-reviewed publication, no mention of a proper data package. The last timeline was shared on August 5th, stating an end of P2 FDA meeting in 4Q19/1Q20, and 1Q20 start for P3 in EG/EGE and P2/P3 in EoE. We wonder if this meeting has occurred, when these trials will start, and what they will look like – will the FDA allow the pivotal trials to be an ENIGMA-like farce, or will reality catch up to Allakos? We noted Facebook posts that share troubling endoscopic findings of patients in the AK002 EG/EGE extension study – patients on drug for as long as a year. If the FDA requires endoscopic endpoints in the P3 design, we expect investors will demand endoscopy data from P2 – which investigators indicate was collected, but which the company has withheld.

> ***"The data set is obviously incomplete. Things are not included****. There's no histology or endoscopic reporting. No biomarkers. I'm sure it was collected. I'd be surprised if it wasn't collected as typically it would be…****The FDA will use endoscopic findings more than eosinophil levels [in phase 3]****. They are very objectively and quantitatively measurable, especially for EoE where there's a score and they're developing one for EG."*
>
> ***– ENIGMA Phase 2 Trial Investigator/KOL familiar with the FDA's approach to eosinophilic gastrointestinal disease (EGID) trials, commenting on ALLK's superficial P2 endpoints and his opinion on likely P3 design.***

> ***"Endoscopic data were collected but haven't been released yet."***
>
> ***– Another ENIGMA trial investigator/KOL***

Source: Seligman expert consultations; ALLK website, press releases, and SEC flings

Introduction to Allakos

In the interim, we caution that Allakos is a gastroenterology company with a phase 2 trial – and note the absence of acquisitions remotely near this market cap which are not in oncology or gene therapy, or after a mere P2. Historical deal tables are easily found in sell-side notes, and we find the color below from an ENIGMA trial investigator more illuminating – and consistent with the poor attendance at ALLK's presentations in late Oct at UEG and ACG:

"I haven't seen anything like this before. Scientifically they are relatively weak. There's been no chatter in our field about their trial results. No one follows this company. *There are not a lot of research scientists involved. No one's sent me any emails, no questions. Since their results came out, there's been no discussion. No one's talked about it. Normally patients even go nuts and send me emails. No one's said anything about it.* ***I am skeptical. I personally don't know how this could be worth billions. It's crazy."***

– Allakos ENIGMA Phase 2 Trial Investigator and KOL in the EGID space

Source: Seligman expert consultations

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Executive summary

	Pages
Introduction to Allakos	*8-22*
22 WARNING SIGNS FOR INVESTORS:	
1. ***The failure of AK001, the precursor to Allakos' lead AK002 program and the canary in the coal mine. AK001/AK002 are virtually identical Siglec-8 antibodies. The company has buried the results for the two AK001 studies it conducted, but our research indicates a debacle - followed by its lead pre-ipo investor dumping its entire stake at $2.48/share in August 2017; the company valuing itself at 93 cents/share weeks later, suggesting a valuation range of $31-83MM; cash dwindling to two months, requiring a bailout by remaining investors; and a new CEO, COO, CFO, CMO, and VP Clinical Ops. Yet a mere 11 months after this chaos, ALLK was re-packaged around "AK002" and a new, questionable phase 1 study in *healthy* volunteers and taken public – a benchmark feat of Wall Street hocus-pocus.***	*23-33*
2. ***Allakos has a checkered history of conducting small, low-credibility trials, marked by a striking level of what we consider to be discrepancies, omissions, cherry-picking, and other red flags.***	*34-46*
3. ***The company appears to have conducted the ENIGMA phase 2 EG/EGE trial itself and served as its "own CRO," with at least four different trial investigators expressing concerns around the company's conduct and the trial's integrity and compliance, describing it as "aggressive," "stupid," "dishonest," or as something that "won't fly with the FDA," and their own reactions as "shocked" and "very bothered." Based on investigators' concerns, we conducted further due diligence on whether biopsies were sent to the company itself or a panel of independent, third-party pathologists – and are troubled by what we found.***	*47-55*
4. ***Flagrant nepotism in key clinical roles, filled by the Chief Medical Officer's son and daughter. The daughter's profile states "class of 2012" in college. The children received options for 100k shares, worth ~$13MM at $130/share. We question why a public company didn't pick more qualified executives for its core function, and note the unusual geographic location of all three family members relative to Allakos' only listed office.***	*56-61*
5. ***Poor controls as well as Allakos' role in running the study itself rendered the ENIGMA trial – purportedly randomized and double-blind - essentially unblinded, making the already subjective endpoint of patient-reported symptom scores a sham. The FDA has cautioned that "Suspicion of inadvertent unblinding can be a problematic review consideration for the FDA when assessing PRO endpoints." Shockingly, a parent posted about speaking to Allakos - the co-founder plus what we infer to be contact with the CMO - which if true would strike us as reckless and raise concerns about trial tampering and Allakos' conduct in general.***	*62-77*

Warning sign #1: The failure of AK001, the precursor to Allakos' lead AK002 program and the canary in the coal mine. AK001/AK002 are virtually identical Siglec-8 antibodies. The company has buried the results for the two AK001 studies it conducted, but our research indicates a debacle - followed by its lead pre-ipo investor dumping its entire stake at $2.48/share in August 2017; the company valuing itself at 93 cents/share weeks later, suggesting a valuation range of $31-83MM; cash dwindling to two months, requiring a bailout by remaining investors; and a new CEO, COO, CFO, CMO, and VP Clinical Ops. Yet a mere 11 months after this chaos, ALLK was re-packaged around "AK002" and a new, questionable phase 1 study in *healthy* volunteers and taken public – a benchmark feat of Wall Street hocus-pocus.

Given that AK001 and AK002 were in simultaneous development, Allakos' decision to first advance AK001 into clinical studies suggests it had evidence indicating better inhibition. If the compound they seem to have believed was the better bet flopped spectacularly in phase 2, the questions for AK002 - as well as the entire Siglec-8 premise – become uncomfortable.

The failure of AK001 in 2017 was an existential event that threw Allakos into crisis. We emphasize that this occurred roughly 11 months prior to IPO in July 2018. If a public biotech company halted the only meaningful trial for its lead compound, after which its lead investor fled, followed by a CEO departure and a new COO, CFO, CMO, and VP Clinical Operations, we'd expect the stock to plummet 90%. Yet Allakos now sports a share price 50-100x greater than the $2.48/share or 93 cent/share benchmarks around Aug 2017.

Allakos is among the greatest rising-from-the-ashes stories in biotech history. The speed of the reversal from Siglec-8 fiasco to Siglec-8 victory has been swift – and worthy of investigation.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

Allakos lists 8 studies on ClinicalTrials.gov, summarized below in rough chronological order. We begin with the two for AK001 before investigating those for AK002.

Start – Completion Date	Drug	Official Title Per ClinicalTrials.gov
Sep 2015 – Mar 2016	**AK001**	A Phase 1, Randomized, Double-Blind, Controlled, Single Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AK001 in Subjects With Atopic Disease https://clinicaltrials.gov/ct2/show/NCT02563938?term=allakos&draw=1&rank=4
Apr 2016 – Jan 2018	**AK001**	A Phase 2, Randomized, Double-blind, Placebo-controlled, Study to Evaluate Multiple Doses of AK001 in Patients With Moderate to Severe Nasal Polyposis https://clinicaltrials.gov/ct2/show/NCT02734849?term=allakos&draw=1&rank=8
Aug 2016 – May 2017	**AK002**	A Phase 1, Double-Blind, Placebo-Controlled, Single Ascending and Multi Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of AK002 in Healthy Participants https://clinicaltrials.gov/ct2/show/NCT02859701?term=allakos&draw=1&rank=6
Jun 2016 – Dec 2018	**AK002**	A Phase 1, Single Ascending Dose and Multiple Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AK002 in Patients With Indolent Systemic Mastocytosis https://clinicaltrials.gov/ct2/show/NCT02808793?term=allakos&draw=1&rank=7
Jan 2018 – Nov 2018	**AK002**	An Open-Label, Pilot Study to Assess the Efficacy and Safety of AK002 (Siglec-8) in Subjects With Antihistamine-Resistant Chronic Urticaria https://clinicaltrials.gov/ct2/show/NCT03436797?term=allakos&draw=1&rank=3
Feb 2018 – Aug 2019	**AK002**	A Phase 1b, Open-Label, Multiple Dose, Proof-of-Concept Study to Evaluate the Safety, Tolerability, and Pharmacodynamics of AK002 in Patients With Atopic Keratoconjunctivitis, Vernal Keratoconjunctivitis, and Perennial Allergic Conjunctivitis https://clinicaltrials.gov/ct2/show/NCT03379311?term=allakos&draw=1&rank=5
Jul 2018 – Jun 2019	**AK002**	A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacodynamic Effect of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis https://clinicaltrials.gov/ct2/show/NCT03496571?term=allakos&draw=1&rank=2
Nov 2018 – Apr 2020E	**AK002**	A Phase 2, Multicenter, Open-Label, Extension Study to Evaluate the Safety and Tolerability of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis https://clinicaltrials.gov/ct2/show/NCT03664960?term=allakos&draw=1&rank=1

Source: ClinicalTrials.gov

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

Allakos strikes us as having gone to great lengths to prevent investors from discovering the outcomes of the two studies for AK001. We understand the reticence, as both AK001 and AK0002 are essentially identical antibodies that bind to Siglec-8. If AK001 was an abject flop, that could create uncomfortable questions for AK002 and the entire Siglec-8 mechanism of action upon which Allakos is premised. We found nothing in Allakos' S-1 or subsequent filings that mention either AK001 study, nor any AK001 data, posters, or publications on the ALLK website or in their other materials. We found a description of AK001 in a 2016 press release – not available on ALLK's site – which begs the question, how is AK001 any different from AK002 as a Siglec-8 antibody?

January 2016 press release states that dosing completed in phase one AK001 study in atopic disease. The study design suggests the generation of material data on the Siglec-8 hypothesis.

"The randomized, double-blind, placebo-controlled, single-ascending-dose study enrolled 34 subjects *to evaluate the safety, tolerability and pharmacokinetics of AK001 in a range of potentially active doses and to obtain early signals of pharmacodynamic activity." – Press release 1/19/2016*

Description of AK001 in press release sounds virtually identical to AK002 description in 8/5/19 release

"AK001 is a therapeutic antibody that targets a receptor present on eosinophils and mast cells. Binding of antibody to this receptor causes inhibition of mast cell activity and selective depletion of activated eosinophils. AK001's action is highly specific to mast cells and eosinophils *and has potential to be of benefit in a wide spectrum of conditions where these cells are involved. AK001 has demonstrated activity in proprietary pre-clinical models of severe allergic diseases." – Press release 1/19/2016*

"The Company's lead antibody, AK002, targets Siglec-8, an inhibitory receptor selectively expressed on human mast cells and eosinophils. AK002 has been shown to inhibit mast cells and deplete eosinophils." *– Press release 8/5/2019*

Source: https://www.rivervest.com/allakos-successfully-completes-dosing-in-phase-1-clinical-trial-of-ak001-and-announces-expansion-of-its-executive-team/; http://investor.allakos.com/news-releases/news-release-details/allakos-announces-ak002-met-all-prespecified-primary-and

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

The Allakos S-1 was artfully written to avoid specific mention of either AK001 study, with amazingly vague disclosure of AK001 at all. The company appears to have begun work on AK001 and AK002 simultaneously, and chose to advance AK001 first – clearly suggesting that their pre-clinical data showed greater activity than AK002. Common sense would dictate that AK001 was discontinued because the first two studies were a bust. If AK001 was trialed first because it showed greater inhibitory activity, and still flopped, we wonder what that indicates for AK002.

Allakos S-1 is nebulous about AK001

"We initially began developing two product candidates, AK001 and AK002, both of which are monoclonal antibodies targeting Siglec-8. *These compounds entered clinical trials in 2015 and 2016, respectively.* ***Due to the greater activity of AK002****, we decided to focus our development efforts on AK002 and* ***discontinued the development of AK001 in 2017."*** *– Allakos S-1 filed July 17, 2018*

The most material clinical data available at the time of IPO in July 2018 would be for AK001. Given that AK001 was discontinued in 2017, we are surprised at the S-1's lack of candor about the two AK001 studies and their results. ***We can imagine no disclosure for an early-stage biotech which is more relevant and material to investors than the failure of its key clinical trials to date. We are amazed that Allakos managed to IPO with such brief and obscure language – especially as this information would have been available to its lead pre-IPO investor, which chose to then exit its entire stake*** *just 11 months before the IPO at a fire-sale price.*

Source: ALLK S-1 filing

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

Although we can find no results for the AK001 atopic disease study, we managed to locate information on the second AK001 study, a phase 2 in nasal polypsis, on the EU Clinical Trials Register. The results indicate that the study was a disaster and was halted early after 40 of 70 patients were enrolled. The then-CEO departed in what appears to have been a board-driven purge of the executive team.

Clinical Trial Results:
A Phase 2, Randomized, Double-Blind, Placebo Controlled, Study to Evaluate Multiple Doses of AK001 in Patients With Moderate to Severe Nasal Polyposis

Summary	
EudraCT number	2016-000460-42
Trial protocol	BE GB ES NL DE
Global end of trial date	05 Jan 2018
Results information	
Results version number	v1(current)
This version publication date	20 Jan 2019
First version publication date	20 Jan 2019
Other versions	

Primary: Change in total polyp score (TPS) Top of page

End point title	Change in total polyp score (TPS) [1]
End point description	
End point type	Primary
End point timeframe	Change in TPS from Baseline (prior to the first dose) to Week 12 (Day 84).

Notes
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The study was terminated early because the Sponsor decided not to pursue further development of AK001 and was, consequently, underpowered for the endpoint comparison. Statistical analyses of the primary endpoint did not show statistically significant results for either the comparison of the 25 mg or the 250 mg group with placebo.

End point values	25 mg AK001	250 mg AK001	Placebo
Number of subjects analysed	15	14	10
Units: score			
least squares mean (confidence interval 95%)	-0.5 (-1.3 to 0.3)	-0.3 (-1.1 to 0.5)	-0.2 (-1.1 to 0.7)

After 40 of the 70 patients planned were randomized in the study, enrollment was stopped as the Sponsor decided not to pursue further development of AK001. The study was not stopped for any safety concern.

Source: https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-000460-42/results; red ours for emphasis

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

We find the failure notable given that Allakos' then-CEO touted the eosinophil and mast cell-enriched nature of nasal polyps, making them the perfect target for a Siglec-8 inhibitor. We find it further notable for the adverse events profile. Although the EU entry specifically calls out that the trial was not terminated early for safety concerns, we wonder if the need to emphasize this is the tell. While the placebo arm indicates a similar percentage of AE's, the distribution tends to minor ones whereas active arm AE's suggest that AK001 completely backfired in the very symptoms that matter: nasopharyngitis, rhinitis, upper respiratory tract infection, lymphadenopathy, asthma, dyspnea, nasal congestion, nasal obstruction, and facial pain.

"Advancing AK001 into a Phase 2 clinical trial in patients is an important milestone …" said Chris Bebbington Ph.D., Chief Executive Officer of Allakos [...] ***"The novel mechanism by which AK001 works is ideally suited for the treatment of nasal polyps, which are highly enriched for eosinophils and mast cells."*** *– Press release 9/8/2016*

Frequency threshold for reporting non-serious adverse events: 0%			
Non-serious adverse events	25 mg AX001	250 mg AX001	Placebo
Total subjects affected by non serious adverse events			
subjects affected / exposed	11 / 15 (73.33%)	10 / 14 (71.43%)	7 / 10 (70.00%)
Nasopharyngitis			
subjects affected / exposed	4 / 15 (26.67%)	2 / 14 (14.29%)	1 / 10 (10.00%)
Upper respiratory tract infection			
subjects affected / exposed	3 / 15 (20.00%)	0 / 14 (0.00%)	0 / 10 (0.00%)
Nasal obstruction			
subjects affected / exposed	3 / 15 (20.00%)	0 / 14 (0.00%)	0 / 10 (0.00%)
Nasal congestion			
subjects affected / exposed	2 / 15 (13.33%)	2 / 14 (14.29%)	0 / 10 (0.00%)

Source: https://www.rivervest.com/allakos-initiates-phase-2-trial-of-ak001-in-patients-with-nasal-polyposis/; https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-000460-42/results; red outs for emphasis

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

The failure of AK001 appears to have been a critical and existential event for Allakos. We believe the company realized sometime in 2H 2016 or early 2017 that AK001 was a dud. Its lead investor indicated in May 2017 that it would not invest any further capital, and a few months later presumably the same investor dumped its entire stake at $2.48/share. Two weeks later the board replaced the CEO and co-founder, and appointed a new COO, CFO, CMO, and VP Clinical Operations – suggestive of a company in freefall.

Lead pre-IPO investor indicated that it would not invest any further capital and that it was seeking to liquidate its entire stake.

*"**In late May 2017, one of the Company's lead investors indicated that it would not invest any additional capital in the Company and notified the Company of its intention to seek to sell its entire equity interest in the Company.** The loss of this lead investor and the impact of its efforts to sell its equity stake were expected to have a **negative impact on the Company's ability to raise a new round of financing."** – Correspondence with SEC pre-IPO by ALLK's lawyers,*
https://www.sec.gov/Archives/edgar/data/1564824/000119312518200129/filename1.htm

In August 2017, presumably the same lead investor exited its stake at $2.48/share.

"On August 3, 2017, one of the Company's lead investors successfully completed the sale of all of its shares of Series A preferred stock in an arms-length transaction at approximately $2.48 per share." – Correspondence with SEC pre-IPO by ALLK's lawyers,
https://www.sec.gov/Archives/edgar/data/1564824/000119312518200129/filename1.htm

Two weeks later, ALLK announced that the board replaced the CEO and co-founder and appointed a new COO and CFO. A new Chief Medical Officer and VP Clinical Ops joined as well – a total overhaul and reset indicative of a company that was floundering.


Allakos Announces Additions to Senior Leadership Team

– Board of Directors appoints Robert Alexander as CEO and Adam Tomasi as COO & CFO –
– Allakos plans to initiate a broad, multi-indication clinical program with AK002 in 2017 –

Source: https://www.allakos.com/news/press-release/081517/

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

Correspondence between Allakos' lawyers and the SEC provided further color on the company's turbulent internal dynamics just months before the IPO – and why the lawyers requested FOIA confidential treatment of their letter. The letter reveals that at the time of the shift to AK002 following the failure of AK001 in June 2017, the company didn't even have a lead indication defined for AK002. It reveals that in August 2017 – we repeat, 11 months before the IPO – the company was down to two months of cash and had to conduct a bridge with existing investors. The company valued itself at 93 cents/share on Aug 31, 2017 – a notable haircut from the $2.48/share its lead investor fled with a few weeks prior.

"In connection with the management team transition, the Company reevaluated its lead product candidate at the time, AK001. ***In June 2017****, due to the greater activity of the Company's other product candidate, AK002, as compared to AK001, the Company decided to focus its development efforts on AK002 and discontinued the development of AK001.* ***At this time, as a result of the shift to AK002, the Company had no lead indication identified."***

"During this time frame the Company's cash resources continued to dwindle, which constrained its activities and limited its plans. ***At one point, in August 2017, the Company's cash resources were sufficient only to support two more months of operations and required the Company to conduct a bridge financing with its existing investors."***

"August 31, 2017 Valuation…The resulting estimated fair value of the Company's common stock was $0.93 per share…"

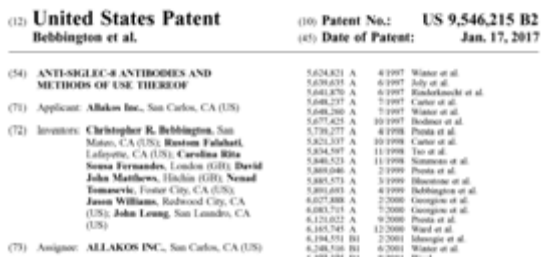
Source: SEC correspondence https://sec.report/Document/0001193125-18-200129/

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

If a public biotech company halted the only meaningful trial for its lead compound, after which its lead investor liquidated its entire stake, followed abruptly by the departure of its CEO and a new COO, CFO, CMO, and VP Clinical Operations, we'd expect the stock to plummet 90%. Yet, 11 months later with just a phase 1 study in healthy volunteers and "promising preclinical animal data in December 2017 in a mouse model of the lead indication of EG/EGE", ALLK's underwriters still managed to take it public in July 2018 with a day-one close of $35 – a benchmark feat of Wall Street hocus-pocus given the valuations between 93 cents and $2.48 in Aug 2017. Irrespective, we believe that Allakos' reticence to provide detail on AK001 points to a far larger problem: there is no meaningful difference between AK001 and AK002. Both are antibodies targeting Siglec-8. Given AK001's failure, Allakos could never have gone public without a "new" compound around which to build a story.

- The company's lack of candor renders the purported difference between AK001 and AK002 a mystery. Given that both Siglec-8 antibodies were in development at the same time, the decision to prioritize AK001 for clinical trials clearly suggests Allakos had data indicating superior anti-eosinophilic activity than AK002.
- **In order to unravel the mystery of AK001 vs. AK002, we examined Allakos' patent filing.** The key patent – *"Anti-Siglec-8 Antibodies And Methods Of Use Thereof"* – references an IgG4 humanized antibody and an afucosylated IgG1 humanized antibody. **We spoke with a former employee of Allakos who indicated that AK001 is the IgG4 Siglec-8-binding antibody, and AK002 is the IgG1 Siglec-8-binding antibody.**



(12) **United States Patent**
Bebbington et al.

(10) **Patent No.: US 9,546,215 B2**
(45) **Date of Patent: Jan. 17, 2017**

(54) **ANTI-SIGLEC-8 ANTIBODIES AND METHODS OF USE THEREOF**

(71) Applicant: **Allakos Inc.**, San Carlos, CA (US)

(72) Inventors: **Christopher R. Bebbington**, San Mateo, CA (US); **Rustom Falahati**, Lafayette, CA (US); **Carolina Rita Sousa Fernandes**, London (GB); **David John Matthews**, Hitchin (GB); **Nenad Tomasevic**, Foster City, CA (US); **Jason Williams**, Redwood City, CA (US); **John Leung**, San Leandro, CA (US)

(73) Assignee: **ALLAKOS INC.**, San Carlos, CA (US)

What is claimed is:

1. An antibody that binds to a human Siglec-8, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:6 or the light chain variable region comprises the amino acid sequence of SEQ ID NOs:16 or 21.

2. The antibody of claim 1, wherein the antibody comprises a heavy chain Fc region comprising a human IgG Fc region.

3. The antibody of claim 2, wherein the human IgG Fc region comprises a human IgG1 or a human IgG4.

Source: Bloomberg; https://sec.report/Document/0001193125-18-200129; https://patentimages.storage.googleapis.com/cf/56/74/4d8edce6d6fc6f/US9546215.pdf

Warning sign #1: The failure of AK001, the canary in the coal mine for AK002

Given that both are antibodies targeting the same receptor, the explanation that AK002 exhibits "greater activity" strikes us as contrived and implausible. Allakos appears to have admitted as much, as we located a 2019 paper by the co-founder plus the CSO/ex-CEO and other ALLK staff which compared the anti-Siglec-8 activity of an IgG1 ("AK002") vs. IgG4 ("AK001") antibody on eosinophils. Not surprisingly, the study indicated that both versions of the antibody exhibited virtually identical levels of activity on eosinophils – a troubling fact for those who believe that AK002 is meaningfully different than the failed AK001 program.

Translational and clinical immunology

Sialic acid–binding immunoglobulin-like lectin (Siglec) 8 in patients with eosinophilic disorders: Receptor expression and targeting using chimeric antibodies

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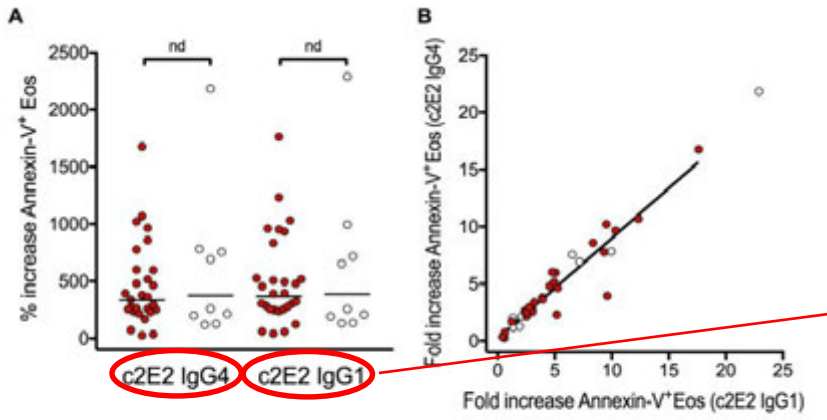


FIG E5. **A**, Apoptosis induced by c2E2 IgG_4 and c2E2 IgG_1 is similar in purified cells from NDs *(white circles)* and EOs *(red circles)* in the presence of IL-5. *nd*, Not determined. **B**, Apoptosis induced by c2E2 IgG_4 and c2E2 IgG_1 is highly correlated in NDs and EOs. The fold increase in Annexin-V^+ eosinophils for an individual subject is calculated with respect to the corresponding value from the isotype control. The *black line* represents a linear regression between the 2 parameters. $R^2 = 0.94$, $P < .0001$.

- Annexin is a marker used to detect cells in apoptasis (cell death). Vertical axis indicates increase in eosinophils in apoptasis
- White circles are healthy subjects and eosinophilic subjects are in red.
- **The plots for IgG4 and IgG1 are essentially identical.**

Source: https://www.jacionline.org/article/S0091-6749(18)31741-X/fulltext

Warning sign #2: Allakos has a checkered history of conducting small, low-credibility trials, marked by a striking level of what we consider to be discrepancies, omissions, cherry-picking, and other red flags.

The ENIGMA phase 2 trial in EG/EGE is the first time the investor community reacted with great enthusiasm to an ALLK trial read-out. We caution investors to closely examine Allakos' previous trials, without which the recent results cannot be properly understood. Such a review points to a clear and troubling pattern, of which the EG/EGE trial is the most extreme example. The pattern is marked by:

1. Spurious study design with single-arm, open-label protocols and small sample sizes. Single arm means there's no placebo control, and open-label means the trial isn't blinded. In other words, study patients and their doctors know the patient is on the drug being studied, and there's nothing to compare it to.

2. A fixation on subjective end-points, where patients report how they feel on a questionnaire ("PRO" or Patient Reported Outcome). Given that patients know they're receiving the drug versus being blinded, such PRO's in an open-label context are biased and worthless except for fluffy, promotional press releases.

3. An ongoing failure in trials to disclose obvious and critical data beyond the PRO, without which even the most basic determination of each trial's outcome cannot be made.

Warning sign #2 (cont'd): Allakos has a checkered history of conducting small, low-credibility trials, marked by a striking level of what we consider to be discrepancies, omissions, cherry-picking, and other red flags.

4. A breathtaking failure to share top-line data on each endpoint for these studies. We cannot recall a biotech company listing several endpoints at the start of a trial, and then failing to specify if the trial even met those endpoints. The only endpoint that Allakos typically releases is – you guessed it – patient-reported outcomes.

5. A pattern of promising that additional data will soon be shared "at an upcoming conference," without it ever subsequently being shared anywhere that we can locate.

What Allakos has historically disclosed is so vague and selective that it would not pass muster for inclusion at a credible medical conference or journal, and would likely be viewed as a farce by the FDA. We wonder what makes the company so reticent. Investors have become enthusiastic that the EG/EGE top-line data is credible as they believe it's the first blinded, placebo-controlled study for which Allakos has released top-line results, while being unaware of the phase 2 dud for AK001. In subsequent sections we detail how the ENIGMA EG/EGE study merely repeats the same Allakos pattern, and in more troubling ways.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

Allakos lists 8 studies on ClinicalTrials.gov, summarized below in rough chronological order. We investigate each of the four AK002 studies preceding ENIGMA and detail a clear pattern.

Start – Completion Date	Drug	Official Title Per ClinicalTrials.gov
Sep 2015 – Mar 2016	**AK001**	A Phase 1, Randomized, Double-Blind, Controlled, Single Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AK001 in Subjects With Atopic Disease https://clinicaltrials.gov/ct2/show/NCT02563938?term=allakos&draw=1&rank=4
Apr 2016 – Jan 2018	**AK001**	A Phase 2, Randomized, Double-blind, Placebo-controlled, Study to Evaluate Multiple Doses of AK001 in Patients With Moderate to Severe Nasal Polyposis https://clinicaltrials.gov/ct2/show/NCT02734849?term=allakos&draw=1&rank=8
Aug 2016 – May 2017	**AK002**	A Phase 1, Double-Blind, Placebo-Controlled, Single Ascending and Multi Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of AK002 in Healthy Participants https://clinicaltrials.gov/ct2/show/NCT02859701?term=allakos&draw=1&rank=6
Jun 2016 – Dec 2018	**AK002**	A Phase 1, Single Ascending Dose and Multiple Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AK002 in Patients With Indolent Systemic Mastocytosis https://clinicaltrials.gov/ct2/show/NCT02808793?term=allakos&draw=1&rank=7
Jan 2018 – Nov 2018	**AK002**	An Open-Label, Pilot Study to Assess the Efficacy and Safety of AK002 (Siglec-8) in Subjects With Antihistamine-Resistant Chronic Urticaria https://clinicaltrials.gov/ct2/show/NCT03436797?term=allakos&draw=1&rank=3
Feb 2018 – Aug 2019	**AK002**	A Phase 1b, Open-Label, Multiple Dose, Proof-of-Concept Study to Evaluate the Safety, Tolerability, and Pharmacodynamics of AK002 in Patients With Atopic Keratoconjunctivitis, Vernal Keratoconjunctivitis, and Perennial Allergic Conjunctivitis https://clinicaltrials.gov/ct2/show/NCT03379311?term=allakos&draw=1&rank=5
Jul 2018 – Jun 2019	**AK002**	A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacodynamic Effect of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis https://clinicaltrials.gov/ct2/show/NCT03496571?term=allakos&draw=1&rank=2
Nov 2018 – Apr 2020E	**AK002**	A Phase 2, Multicenter, Open-Label, Extension Study to Evaluate the Safety and Tolerability of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis https://clinicaltrials.gov/ct2/show/NCT03664960?term=allakos&draw=1&rank=1

Source: ClinicalTrials.gov

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

The shift to AK002 began with a phase 1 study to evaluate the compound's activity. Allakos states that all doses "resulted in complete depletion of blood eosinophils one hour after administration" – an exciting claim that has convinced investors of AK002's anti-eosinophil properties. Upon closer examination, however, the study raises more questions than it answers, and the data disclosed is so sparse and selective that we consider it a farce.

Why were only healthy volunteers tested **versus patients with elevated eosinophils?**

The company must have collected data on tissue eosinophil levels, **yet shows only blood eosinophils.**

The trial lasted 112 days, yet blood eosinophil levels are shown for **only one arbitrary interval – 1 hour post-infusion**. What happened to eosinophil levels after 1 day, 1 week, 1 month, etc?

Clinical Results

AK002 was tested in a randomized, double-blind, placebo-controlled, dose-escalating Phase 1 trial conducted in Melbourne, Australia. 51 healthy volunteers were randomized to receive doses of AK002 (0.001, 0.003, 0.01, 0.03, 0.1, 0.3, or 1.0 mg/kg) or placebo. The primary endpoints of the trial were safety and tolerability. The secondary endpoints included pharmacokinetic and pharmacodynamic ("PK/PD") measurements, including changes in the absolute peripheral blood counts of eosinophils.

As shown in Figure 5, with respect to the secondary endpoints, all doses of AK002 tested resulted in complete depletion of blood eosinophils one hour after administration, clearly demonstrating the pharmacodynamic activity of AK002. The duration of depletion was dose-dependent with a single dose of 1.0 mg/kg of AK002 suppressing eosinophils for up to 84 days. AK002's pharmacokinetic half-life was determined to be 18 days.

Figure 5. Single Dose Placebo and AK002 Eosinophil Response

	Blood Eosinophils 10^3/mL				
Dose Cohort (mg/kg)	Placebo Pre-dose	Placebo 1 Hr Post-dose	AK002 Pre-dose	AK002 1 Hr Post-dose	Minimal Duration Eos Depletion
0.001	NA	NA	70	0	1 Day
0.003	120	70	160	0	2 Days
0.01	210	150	160	0	4-7 Days
0.03	150	150	160	0	7-14 Days
0.1	100	80	250	0	14-28 Days
0.3	180	140	180	0	28 Days
1.0	60	40	120	0	56-84 Days

Where's the multi-dose data - did dose escalation impact safety? What did dose-response curve look like?

Steroids drive dramatic eosinophil reductions and are a confounding factor - were they administered prior to infusion as in ENIGMA?

Impossible to determine the meaning of "minimal duration eos depletion".

Source: Allakos S-1 filing , https://www.sec.gov/Archives/edgar/data/1564824/000119312518219134/d447521ds1a.htm; red outs for emphasis.

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

We find Allakos next trial – a phase 1 evaluating AK002 in indolent systemic mastocytosis (ISM) – just as questionable, continuing the company's pattern of small, open-label trials with selective and troubling levels of disclosure. Shockingly, the top-line press release for the trial in February 2019 declared the results "positive" yet failed to state whether AK002 reduced eosinophil or mast cell levels, despite such histologic response rates being outcome measures. We find this absurd as the release even states that "Indolent systemic mastocytosis (ISM) is a disorder caused by increased numbers and activation of mast cells throughout the body." We see no reason for the failure to disclose unless AK002 failed to impact eosinophil and mast cell counts.

Red flags

1. **Open-label, single-arm trial with only 25 participants** per ClinicalTrials.gov

Study Design Go to

Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	25 participants
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase 1, Single Ascending Dose and Multiple Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AK002 in Patients With Indolent Systemic Mastocytosis
Actual Study Start Date :	June 2016
Actual Primary Completion Date :	December 2018
Actual Study Completion Date :	December 2018

Source: https://clinicaltrials.gov/ct2/show/NCT02808793?term=allakos&draw=1&rank=7

2. The trial specified various histologic outcome measures such as **eosinophil and basophil (similar to mast cells) levels, yet Allakos' press release was conspicuously silent on the results.**

> 2. Evaluate the change from baseline in absolute peripheral counts of eosinophils and basophils. [Time Frame: Through out the study from screening to Day 85 or early term visit]

Source: https://clinicaltrials.gov/ct2/show/NCT02808793?term=allakos&draw=1&rank=7; red outs for emphasis.

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

Red flags continued (2/3): Phase 1 trial evaluating AK002 in indolent systemic mastocytosis

3. The press release provided data for **only the multiple-dose cohort with a mere 11 patients**, leaving out detail for the patients in the single ascending dose cohort. **The obvious implication is that the other cohort failed, even using the low bar of PRO's in an unmasked trial setting.** The opening sentence of the releases states *"Allakos Inc. (NASDAQ: ALLK), a biotechnology company developing AK002 for the treatment of eosinophil and mast cell related diseases, today announced positive **multiple dose** Phase 1 results in patients with indolent systemic mastocytosis (ISM), a debilitating disorder caused by the release of inflammatory mediators from mast cells."* *(press release:* http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-1-results-ak002-indolent)

4. In place of mast cell reduction or other histologic data, the only "data" presented is median change from baseline based on three symptom questionnaires, **exhibiting the company's ongoing fixation on subjective, unreliable PRO's** (patient-reported outcome measures) versus more credible evidence of efficacy. **Comically, N=8 in the table below.**

MSQ Symptom (N=8) *	Median Change from Baseline at Weeks 21 to 22
Hives	-56%
Flushing (#)	-38%
Abdominal Pain	-46%
Diarrhea	-60%
Itching	-49%
Headache	-50%
Fatigue	-47%
Difficulty Concentrating	-59%
Muscle Pain	-27%
Joint Pain	-26%

* The MSQ was not available for use in 3 patients

Press release: http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-1-results-ak002-indolent; red ours for emphasis.

5. **Even the sparse PRO data presented is suspect.** Note the asterisk we have circled above stating that "*The MSQ [Mastocytosis Questionnaire – brackets ours] was not available for use in 3 patients" – a mysteriously-phrased caveat. **Historically, we have found these types of unexplained exclusions to be indicative of cherry-picking in order to fabricate positive study results.** Given that N only equals 8, the 3 missing PRO's indicate that over a quarter of the questionnaires weren't even included.

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

Red flags continued (3/3): Phase 1 trial evaluating AK002 in indolent systemic mastocytosis

6. For the third questionnaire used, the company merely provides an outcome summary along 4 categories, perhaps because listing each survey item in the PRO would expose the methodology for what it is. We located the full Mc-QoL PRO in a medical journal, and survey items include **"less capable," "choice of clothes," "uncomfortable in public," "burdened by symptoms," "fear of wrong treatment," and "feel concerned"** – more appropriate for a science fair than a robust clinical trial.

MC-QoL Domain (N=11)	Median Change from Baseline at Weeks 21 to 22
Symptoms	-39%
Social Life / Functioning	-42%
Emotions	-57%
Skin	-44%

Press release: http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-1-results-ak002-indolent,

Mc-QOL PRO: https://www.ncbi.nlm.nih.gov/pubmed/26797792

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

Around the time of the Phase 1 mastocytosis "read-out" earlier this year, Allakos trickled out a series of press releases with top-line results for its Phase2a AK002 trial in chronic urticaria (hives or skin rash). Yet another small study lacking a control arm, the company's claims and cherrypicked disclosure strike us as suspicious. The market seems to have agreed, with the stock falling 9% with the first press release on January 7th 2019 and 30% overall by the third urticaria results release in mid-February.

- The study included four urticaria cohorts, each with **miniscule sample size**: Xolair-naïve (**n=13**), cholinergic urticaria (**n=11**), dermatographic urticaria (**n=10**), and Xolair refractory chronic spontaneous urticaria (**n=11**).
- **Antihistamines are a frontline treatment for urticaria, yet patients were allowed to use them during the study**, making it impossible to assess the impact of AK002 vs. antihistamines and rendering the study useless. Steroids, another urticaria treament[1] and confounding factor, also appear to have been allowed.
- The press releases began with "data" on the Xolair-naïve subgroup[2]. The only primary outcome measure is **once again a patient survey** to measure urticaria symptoms, **without any information shared about AK002's effect on mast cells**, despite their role as the primary effector cell for the condition[3]. Refusal to disclose any histologic response rates – even directional – is a consistent and worrisome pattern.
- The study used three different surveys/PRO's yet the release disclosed response rates from only one, the Urticaria Control Test (UCT). **We wonder why similar data was withheld for the other clinical tools employed**, the UAS7 (Urticaria Activity Score) and AE-QoL (Angioedema Quality of Life Questionnaire).
  - We find it unusual that the principal investigator for the study, Marcus Maurer, is also listed in a paper[4] as having helped develop the UCT instrument, e.g., he's using his own scale to assess the outcome of a study he's being paid to conduct.
  - While the release touts complete response rates of 92% using UCT scores**, the methodology lacks credibility, using a misleading definition of "complete response"** which is actually a relative response reported by the patient vs. the physician: *"UCT complete response was defined as a greater than 3-point improvement from baseline and a score of 12 or greater."*[3]

Sources: [1]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4248510/ ; [2]http://investor.allakos.com/news-releases/news-release-details/allakos-announces-positive-phase-2-results-cohort-xolair-naive; [3]https://www.ncbi.nlm.nih.gov/pubmed/29431202; [4] https://www.ncbi.nlm.nih.gov/pubmed/24522090

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

Following the read-outs for the urticaria and mastocytosis trials in Jan/Feb 2019, Allakos reported "positive" results for its severe allergic conjunctivitis (SAC) trial in May – the last results before the EG/EGE read-out in August. Yet another low-credibility phase 1 study with a tiny sample size (n=29) and no control, Allakos talked up the study results but once again shared little beyond improved scores on subjective questionnaires. The company's press release and presentation provided another master class in omissions, cherry-picking, and spin.

Of many red flags, we note that the trial's endpoints appear to have changed midway. ClinicalTrials.gov states that one of the trial's outcome measures was *"changes from baseline in absolute peripheral blood counts of eosinophils and basophils"* – essential information given the company's claims that elevated eosinophil and mast cell levels cause an inflammatory cascade.

Outcome Measures Go to

Primary Outcome Measures :

1. To evaluate the safety and tolerability by evaluating Clinical laboratory parameters and adverse events assessed using the CTCAE version 4.03
   [Time Frame: Adverse events will be collected starting from the time of first study drug infusion and ending at Day 309 (±7 Days) or the ET Visit unless directed otherwise by Allakos]

Secondary Outcome Measures :

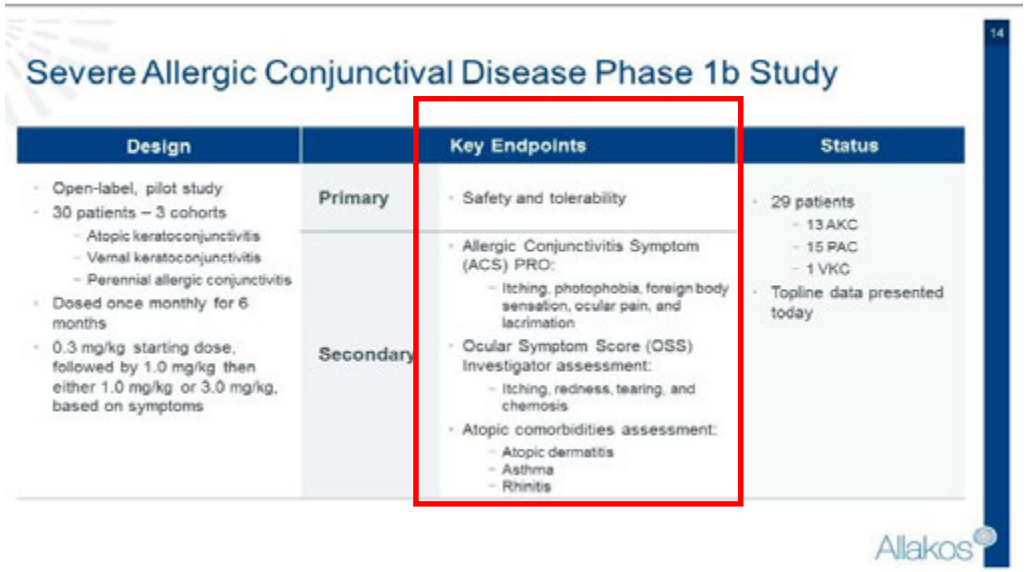
1. To evaluate the pharmacodynamics of AK002 in patients with AKC, VKC, or PAC as measured by changes from baseline in absolute peripheral blood counts of eosinophils and basophils [Time Frame: Starting pre-dose on day -1 to day 309 or early term visit]
2. To evaluate the pharmacodynamics of AK002 using the Allergic Conjunctivitis Symptom Questionnaire (ACS) [Time Frame: Throughout the study from screening to day 309 or early term visit]

   To evaluate the pharmacodynamics of AK002 in patients with AKC, VKC, or PAC as measured by changes from baseline symptoms associated with AKC, VKC, or PAC as measured daily by a disease-specific patient questionnaire, the Allergic Conjunctivitis Symptom Questionnaire (ACS)

Source: https://clinicaltrials.gov/ct2/show/NCT03379311?term=allakos&draw=1&rank=5; red ours for emphasis.

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

Yet when Allakos released the results of the SAC phase 1 in May 2019, the endpoint for eosinophil and mast cell blood counts is curiously missing, replaced by a physician questionnaire instead. On the study results call, the CEO stridently asserted they had shown blood eosinophil reduction, making the now-disappeared endpoint and lack of associated information even more troubling. This is the same pattern as in the mastocytosis study – listing cell levels in blood as an endpoint and then staying radio silent.



"We've recently put out a series of clinical data releases, including today's. ***The upshot is we've shown rapid depletion of blood eosinophils in all of those studies*** *[…] So what we're doing if you go to the right side is our antibody, AK002, will pharmacologically activate the inhibitory function of Siglec-8. So this will antagonize activating signals to the cell.* ***The upshot of this is it kills the eosinophils and broadly inhibits mast cells*** *[…] What we're focused on are mast cells and the eosinophils.* ***And our drug clearly kills eosinophils and does it quite rapidly. What we've also demonstrated is that we have broad inhibition of the mast cell.*** *So what we're trying to do with AK002 is to take mast cells and the eosinophils out of the equation. And by doing that, we would disrupt the inflammatory cascade and allow the tissues to calm down and heal." – Allakos CEO, May 7, 2019 results call (source: Capital IQ/Bloomberg transcripts)*

Source: Allakos 8-k filing https://www.sec.gov/Archives/edgar/data/1564824/000156459019016591/allk-ex991_7.htm, red box ours for emphasis.

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

Just as worrisome, the trial allowed patients to use other drugs which are treatments for allergic conjunctivitis, including steroids, making it impossible to determine whether these drugs or AK002 drove the purported improvement in symptom scores. We wonder whether patients were also allowed to use Dupixent (dupilumab), given the CEO's less-than-100% certain response when asked for clarification on the study results call.

The trial's inclusion criteria (#5) allowed other conjunctivitis medications as well as dose modification. The exclusion criteria (#10) explicitly carved out an exception for steroid use.

5. Stable dose(s) of allowed AKC, VKC, or PAC medication(s) during the 14 days prior to Day 1; and commitment to remaining on the same dose(s) of AKC, VKC, or PAC medication(s) for the entire duration of study participation (unless dose modification is due to unforeseen medical necessity) per Section 8.1 and Section 8.2.

10. Use during the 30 days before Screening (or 5 half-lives, whichever is longer) or use during the Screening period of topical decongestants, topical vasoconstrictors, topical calcineurin inhibitors, topical corticosteroids*, omalizumab, dupilumab, systemic immunosuppressive drugs, or systemic corticosteroids with a daily dose >10 mg prednisone or equivalent per Section 8.1 and Section 8.2

*Topical corticosteroids for atopic dermatitis, corticosteroid nasal sprays for rhinitis, and inhaled corticosteroids for allergic asthma are allowed.

Source: https://clinicaltrials.gov/ct2/show/NCT03379311?term=allakos&draw=1&rank=5; red ours for emphasis.

In response to a simple question about whether Dupixent was allowed during the trial, the CEO responded twice with his belief versus a straightforward answer with no ambiguity.

Timothy Francis Lugo
And I think you mentioned this in response to Sam's question, but just to make sure I had it correct. The patients who were on DUPI entering this study then who were not on DUPI during the study, and so the benefit we're seeing is not on the top DUPIXENT as well? It's in those patients that have been weaned off it before entering the study?

Robert Alexander, Allakos CEO
Yes. That's right, Tim. I believe there was no -- I believe they're able -- they're allowed to stay on their topical steroids during the study, but not dupilumab or any biologic.

Source: Allakos May 7, 2019 trial results call, Capital IQ/Bloomberg transcripts

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

The SAC trial's design appears to be flawed in another crucial manner. Enrollment began in late February and ended in Sept or early October per ClinicalTrials.gov. Recruitment began just as the peak pollen season kicked off, and ended just as peak allergy season concluded. Given that allergens are a trigger for allergic conjunctivitis, we question whether the trial's questionnaires – lacking a control group – measured nothing more than typical seasonal improvement in allergy symptoms.

Tracked changes in ClinicalTrials.gov indicate trial completed recruitment in Sept/Oct

Changes (Side-by-Side) for Study: NCT03379311
September 12, 2018 (v10) -- October 9, 2018 (v11)

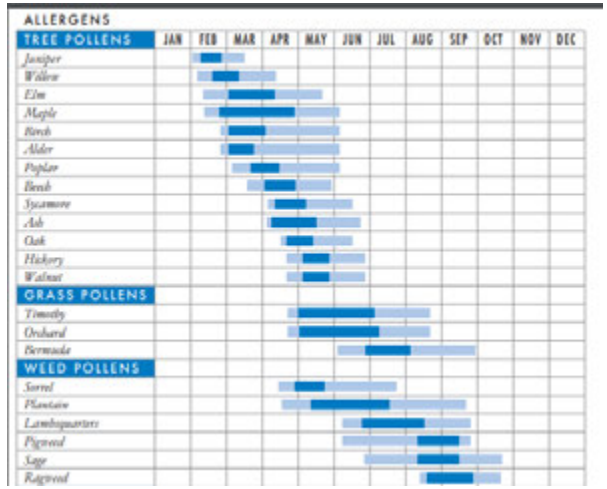
Changes in: Study Status, Contacts/Locations and Study Design

Show only changed modules

	September 12, 2018	October 9, 2018
Study Identification		
Unique Protocol ID:	AK002-005	AK002-005
Brief Title:	A Study of AK002 in Patients With Atopic Keratoconjunctivitis, Vernal Keratoconjunctivitis, and Perennial Allergic Conjunctivitis (KRONOS)	A Study of AK002 in Patients With Atopic Keratoconjunctivitis, Vernal Keratoconjunctivitis, and Perennial Allergic Conjunctivitis (KRONOS)
Official Title:	A Phase 1b, Open-Label, Multiple Dose, Proof-of-Concept Study to Evaluate the Safety, Tolerability, and Pharmacodynamics of AK002 in Patients With Atopic Keratoconjunctivitis, Vernal Keratoconjunctivitis, and Perennial Allergic Conjunctivitis	A Phase 1b, Open-Label, Multiple Dose, Proof-of-Concept Study to Evaluate the Safety, Tolerability, and Pharmacodynamics of AK002 in Patients With Atopic Keratoconjunctivitis, Vernal Keratoconjunctivitis, and Perennial Allergic Conjunctivitis
Secondary IDs:		
Study Status		
Record Verification:	~~September 2018~~	October 2018
Overall Status:	Recruiting	Active, not recruiting
Study Start:	February 26, 2018	February 26, 2018
Primary Completion:	March 2019 [Anticipated]	March 2019 [Anticipated]
Study Completion:	~~March 2019~~ [Anticipated]	August 2019 [Anticipated]

Source: https://clinicaltrials.gov/ct2/history/NCT03379311?A=10&B=11&C=Side-by-Side#StudyPageTop

Peak allergens by type, monthly



Source: Johns Hopkins Division of Allergy and Immunology, http://jhuasthmaallergy.jhmi.edu/allergicreactions/pollen-chartmidatlantic.pdf

American College of Allergy, Asthma, and Immunology states that the first line of treatment is avoiding allergens like pollen

→

Management and Treatment

The first approach in managing seasonal or perennial forms of eye allergy should be to avoid the allergens that trigger your symptoms.

Outdoor exposure

- Stay indoors as much as possible when pollen counts are at their peak, usually during the midmorning and early evening, and when wind is blowing pollens around.
- Avoid using window fans that can draw pollens and molds into the house.
- Wear glasses or sunglasses when outdoors to minimize the amount of pollen getting into your eyes.

Source: https://acaai.org/allergies/types/eye-allergy

Warning sign #2: Allakos has a checkered history of conducting low-credibility trials with numerous red flags

Despite these red flags, Allakos' SAC study results call was promotional featuring two KOL's who appeared to be reading a spoon-fed script, which we found over the top to the point of being unseemly – including the assertion of a "turnaround" of a patient's "systemic disease" within "hours." We note an amusing moment where the principal investigator went off-script during the Q&A and stated that a mere 2% of his practice would be candidates for the drug, contradicting his earlier hyperbole as well as the company's TAM claims, followed by quick tap dancing by the Allakos CEO and COO, who earlier introduced the Harvard immunologist as having developed the standard of care and as the author of "more than 800 peer-reviewed publications and more than 100 books and chapters."

*"The data are **quite striking, quite impressive**. And we, as investigators, **were thunderstruck…"***

***"This is shockingly robust** in terms of reduction and the signs and symptoms…."*

*"So in summary, **you can see that there's definitely impressive clinical activity**…."*

*"**I have not seen something work as nicely as this** […] It's something that's **new and exciting**…."*

*"And the medication itself seems to be **extremely effective** at a very low risk to the patient in our experience thus far, which is also **particularly exciting.**"*

*"**It's neat to see how quickly the medication works**…remembering the first patient enrolled in the study who was particularly miserable and particularly vocal in communicating how miserable he was about the disease. **Within the hours of his infusion was already describing to us how much better he had felt with respect to his allergy. So, a very significant turnaround for him as well as in his systemic disease as well.***

***Analyst:** I was just wondering **what percentage of your SAC patients you will use this drug** and - if it does become available eventually. […] **Stephen Foster: 2% of my practice.**"*

Source: Allakos May 7, 2019 trial results call, Capital IQ/Bloomberg transcripts

Warning sign #3: The company appears to have conducted the ENIGMA phase 2 EG/EGE trial itself and served as its "own CRO," with at least four different trial investigators expressing concerns around the company's conduct and the trial's integrity and compliance, describing it as "aggressive," "stupid," "dishonest," or as something that "won't fly with the FDA," and their own reactions as "shocked" and "very bothered." Based on investigators' concerns, we conducted further due diligence on whether biopsies were sent to the company itself or a panel of independent, third-party pathologists – and are troubled by what we found.

Allakos appears to have served as its own contract research organization (CRO) for this trial, in contrast to standard industry practice, which led physicians who served as trial investigators to express concerns around the company's conduct.

Trial investigators we spoke with appeared to feel duped upon discovering that they had been interacting with Allakos staff vs. CRO employees. One described the company's conduct as "aggressive" and hinted at other concerns which he felt uncomfortable elaborating.

A second investigator was "shocked' and described the behavior as "stupid" from a compliance and audit standpoint and as a red flag that "won't fly with the FDA." A third was "very bothered" and used the word "dishonest."

Given Allakos' unusual and "aggressive" involvement with the study, we conducted further due diligence on whether biopsies were sent to the company itself or a panel of independent, third party pathologists, given well-known issues around bias and subjectivity in biopsy measurements.

Warning sign #3 (cont'd): Allakos appears to have conduced the ENIGMA trial itself versus a CRO

To our surprise, a trial investigator/KOL indicated that a single individual served as the central reader and measured tissue samples for eosinophil and mast cell levels. Our research leads us to believe that the pathologist is someone with financial ties to Allakos, based on a conflict-of-interest disclosure.

CRO's serve as independent third parties to assure a clinical trial's compliance and integrity regarding trial protocol, patient inclusion and exclusion criteria, blinding, and essential audit and assessment standards. Not using an independent third party to provide checks and balances reminds us of a company serving as its own auditor, or a fund serving as its own administrator.

Warning sign #3: Allakos appears to have conducted the ENIGMA trial itself versus a CRO

Our research indicates that the vast majority of clinical trials (>90%) employ a contract research organization, a fact reinforced by Allakos' own trial investigators who indicated that this was the first company-sponsored study they had ever been involved with where the company ran the study themselves and served as its own CRO. We find this odd given statements in the Allakos 10K:

We rely on third-parties to conduct our clinical trials and those third-parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.

We do not have the ability to independently conduct our clinical trials. We currently rely on third-parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of AK002 and expect to continue to rely upon third-parties to conduct additional clinical trials of AK002 and our other product candidates. Third-parties have a significant role in the conduct of our clinical trials and the subsequent collection and analysis of data. These third-parties are not our employees, and except for remedies available to us under our agreements, we have limited ability to control the amount or timing of resources that any such third-party will devote to our clinical trials.

Source: Allakos 10K filed 3/14/2019

Warning sign #3: Allakos appears to have conducted the ENIGMA trial itself versus a CRO

We were first alerted by one of the trial investigators who we consulted as part of our research. This doctor, a prominent KOL (key opinion leader) in the field, assumed that he had been interacting with CRO staff all along and was surprised when he discovered that they were in fact Allakos employees.

The KOL indicated that this was unusual and the company was "aggressive," and hinted at other concerns which he felt uncomfortable elaborating.

"One of the things about this company – they were the CRO for this trial. Which is interesting. They didn't use one. ***This doesn't normally happen. The company was actively involved during the trial. They were involved and aggressive. I don't want to go into subjective things. There were lots of circumstances."***

He stated this was the only time he had seen a biotech company play this role itself

"Companies fall into three categories. One, the company comes in, hires a CRO. The CRO doesn't know what's going on and I know more than CRO and CRO hassles you with details. Two, a company uses a CRO but the company's on top of it and it's a pleasant experience. You deal with knowledgeable people. ***Then the third group, Allakos. N=1. Only this company. It was all company people running the study. It's the only time I was ever involved in a study like this. I've been involved in over two dozen company-sponsored studies. I can't say it was pleasant working with them because they were very self-centered about things."***

He again commented on Allakos staff being "aggressive" and his surprise at discovering they didn't work for a CRO

"They were aggressive. They carried out the study quickly. They got patients fast, and analyzed data in an unbelievably fast manner. All the reps were on top of things. They were very motivated. ***I thought it was unusual. I didn't realize they were their own CRO. I asked them. I asked them, "Which company are you with?" and they said they're employees of Allakos and I was surprised. I'd never seen this before.*** *These guys are businesspeople. They think we made a couple hundred million and this could be one of these."*

Source: Seligman expert consultations

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #3: Allakos appears to have conducted the ENIGMA trial itself versus a CRO

We double-checked our research with a second trial investigator, who also initially assumed that Allakos used a CRO. When we asked him to verify, he asked his staff and confirmed that he had actually been dealing with Allakos employees. He stated he was "shocked" and described Allakos' conduct as problematic from an FDA standpoint.

The doctor indicated this his center always deals with a third party CRO for compliance reasons

"We dealt with someone from Allakos. I assumed it was a third party**. We always deal with a third party CRO that makes sure there's **compliance with internal and external protocols and inclusion/exclusion criteria."

He viewed Allakos' behavior as unusual, "stupid" from a compliance and audit standpoint, and a red flag that "won't fly with the FDA."

*"It should be a third party to prevent bias. **I don't know why they didn't use a third party. I'd say 95% of time it's a third party. It's never the company. We've conducted so many trials**. It's never been the company. It's one of the biases that you definitely want to remove. Inherent bias from internal review shouldn't exist in these trials. **This would be a huge red flag in phase three and the FDA wouldn't like it. They would be stupid to have their own people do compliance, assessment, and auditing. It just won't fly with the FDA."***

He added that he was "shocked," and that he counsels even tiny biotech startups to follow standard operating procedure and use a CRO.

*"We have 130 active studies currently. Just in the past five years, we've probably done 20 trials. Large ones with more than 1,000 people. All twenty of those were with a third party CRO. That's the standard. **That's standard operating procedure. I'm advising very tiny biotech companies, and I'm even telling them, you want a third party CRO.** These are startups. **That's the right thing to do. I was shocked to see that Allakos served as their own CRO."***

Source: Seligman expert consultations

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #3: Allakos appears to have conducted the ENIGMA trial itself versus a CRO

We then asked a third investigator, who was unaware that the center's staff had been interacting with Allakos employees during the trial. The doctor put us on hold and called the nurse who served as the facility's clinical research coordinator. When the nurse confirmed the role of Allakos employees, the doctor's tone abruptly changed into one that we would characterize as somber and disturbed, similar to someone who realizes they've been duped.

The doctor was "very bothered" and felt Allakos' behavior was dishonest

*"I believe the site monitors were employees of Allakos. **I just asked my clinical research coordinator.** The person who came for site visits is an Allakos employee. **My patient coordinator worked directly with Allakos. If it was an Allakos person and not a CRO I'd be very bothered by that. It wouldn't be honest."***

The doctor's clinical research coordinator also mentioned the involvement of a contractor. We asked if the clinical research coordinator could locate this person's card. The card had the person's name with no company affiliation, at which point the doctor became quiet and seemed unsettled. We located the individual's LinkedIn profile, which also failed to list a current company.

*"Monitor visits to check paperwork were a contract person. The name on the card is [name redacted]. **The card doesn't have a company name on it for the CRO."***

Source: Seligman expert consultations

Warning sign #3: Allakos appears to have conducted the ENIGMA trial itself versus a CRO

We also asked a fourth investigator, an influential KOL in the EGID space. Unlike the other investigators, he appeared to know all along that Allakos conducted the study themselves and seemed uncomfortable when we raised the topic. He hypothesized that Allakos "would have" blinded some employees and unblinded others – a notion we find absurd given the small number of employees at Allakos (45 per LinkedIn around study start in mid-2018, 79 as of Dec 2019), not to mention nepotism in key clinical roles as we detail in the next section. Nonetheless, the investigator did not defend Allakos' conduct, highlighted the critical importance of blinding, and stated he didn't know why the company chose this route.

"Allakos mostly did the study themselves and contracted out services as needed. I'm not at liberty to disclose what they did themselves versus contracting out*. Access to the data needs to be very strict. You can only see some things if you're on the blinded team versus the unblinded team.* ***Allakos would have had people who were blinded and not blinded. I can't speak to why they did it this way."*** ***– ENIGMA investigator and KOL***

Source: Seligman expert consultations; LinkedIn

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

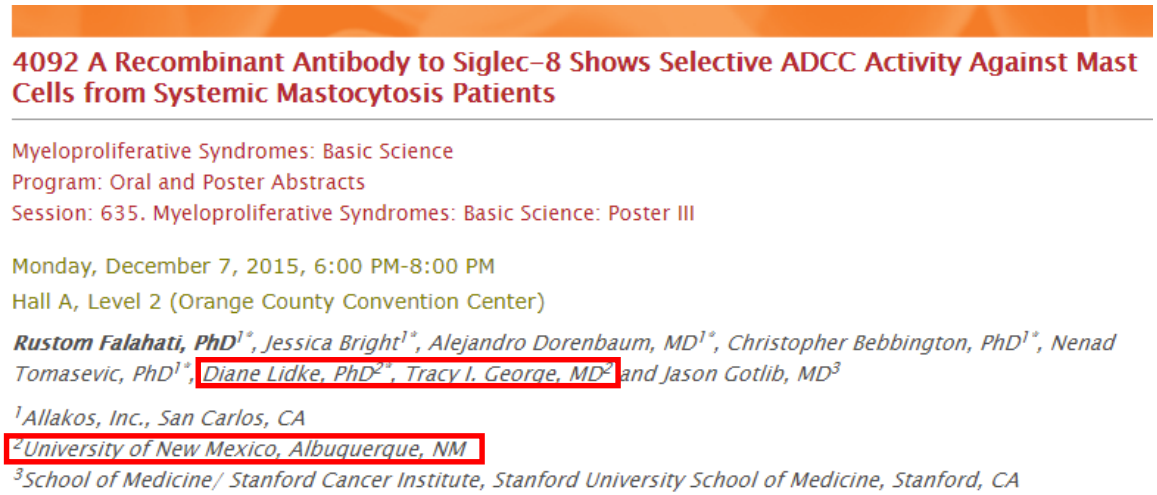
Warning sign #3: Allakos appears to have conducted the ENIGMA trial itself versus a CRO

Allakos role and conduct raises troubling questions about the trial's integrity and compliance. Given its unusual and "aggressive" involvement with the study, we conducted further due diligence on whether biopsies were sent to the company itself or a panel of independent, third party pathologists, given well-known issues around bias and subjectivity in biopsy measurements. To our surprise, a trial investigator and KOL indicated that a single individual served as the central reader and measured tissue samples for eosinophil and mast cell levels.

The investigator indicated that biopsies were sent to one person. We were uncertain from his comments whether this individual was formally an Allakos employee, or merely equivalent to one.

"They had a central reader. It was one person at their company. *Someone who's published in the area. They're fairly well regarded for a* ***company representative****. The person works for a for-profit pathology lab.* ***Everything was done by this person.*** *I don't know the details. You should look at abstracts the company has published. The pathologist is an author on one."*

We followed the KOL's advice and identified the abstract, which lists two pathologists, one of whom we believe to be the one that received biopsies and conducted cell counts under microscope.



4092 A Recombinant Antibody to Siglec–8 Shows Selective ADCC Activity Against Mast Cells from Systemic Mastocytosis Patients

Myeloproliferative Syndromes: Basic Science
Program: Oral and Poster Abstracts
Session: 635. Myeloproliferative Syndromes: Basic Science: Poster III

Monday, December 7, 2015, 6:00 PM-8:00 PM
Hall A, Level 2 (Orange County Convention Center)

Rustom Falahati, PhD[1*], *Jessica Bright*[1*], *Alejandro Dorenbaum, MD*[1*], *Christopher Bebbington, PhD*[1*], *Nenad Tomasevic, PhD*[1*], *Diane Lidke, PhD*[2*], *Tracy I. George, MD*[2] *and Jason Gotlib, MD*[3]

[1]*Allakos, Inc., San Carlos, CA*
[2]*University of New Mexico, Albuquerque, NM*
[3]*School of Medicine/ Stanford Cancer Institute, Stanford University School of Medicine, Stanford, CA*

Source: Seligman expert consultation; abstract link https://ash.confex.com/ash/2015/webprogramscheduler/Paper83985.html; red ours for emphasis.

Warning sign #3: Allakos appears to have conducted the ENIGMA trial itself versus a CRO

Amazingly, both pathologists are recipients of research funding from Allakos, which they list in a 2018 conflict of interest disclosure. Given the obvious conflict of interest, we question the integrity of the tissue eosinophil reductions that Allakos claims in the ENIGMA trial.

Journal List › Blood Adv › v.2(3); 2018 Feb 13 › PMC5812326

blood advances

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Published online 2018 Jan 29.
doi: 10.1182/bloodadvances.2017011551

PMCID: PMC5812326
PMID: 29378725

Variability of PD-L1 expression in mastocytosis

Ellen W. Hatch,[1,*] Mary Beth Geeze,[1,*] Cheyenne Martin,[1] Mohamed E. Salama,[2] Karin Hartmann,[3] Gregor Eisenwort,[4,5] Katharina Blatt,[4,5] Peter Valent,[4,5] Jason Gotlib,[6] Ji-Hyun Lee,[7] Lu Chen,[7] Heather H. Ward,[7,8] Diane S. Lidke,[1,7] and Tracy I. George[1,7]

Conflict-of-interest disclosure: T.I.G. and D.S.L. received research funding from Allakos. T.I.G. and J.G. received consulting fees from Blueprint Medicine. T.I.G., P.V., J.G., and K.H. received consulting fees from Novartis and were on a midostaurin trial study steering committee for Novartis. K.H. received consulting fees from ALK and Deciphera. P.V. received research grants from Deciphera and Blueprint. P.V. and K.H. received a research grant from Novartis. The remaining authors declare no competing financial interests.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5812326/

Warning sign #4: Flagrant nepotism in key clinical roles, filled by the Chief Medical Officer's son and daughter. The daughter's profile states "class of 2012" in college. The children received options for 100k shares, worth ~$13MM at $130/share. We question why a public company didn't pick more qualified executives for its core function, and note the unusual geographic location of all three family members relative to Allakos' only listed office.

The son and daughter of the Chief Medical Officer, Henrik Rasmussen, serve as Director of Clinical Project Management and Clinical Program Manager, respectively, per a related party disclosure on page 155 of the S-1. We find the fact pattern alarming, in the context of other red flags and discrepancies in the conduct of the ENIGMA trial.

In 2017/18 the CMO's two children were awarded options to purchase about 100k shares of stock – at a recent price of $130, 100k shares of stock are worth ~$13 million. An online search states the daughter was "class of 2012" in college. This appears to be her fourth instance of nepotism, having overlapped with the father at three prior roles (ZS Pharma, Rasmussen Biotech & Pharma Consulting, and Nabi Pharmaceuticals, per their respective LinkedIn bios).

Our research leads us to believe the son's title is actually VP Clinical Operations, presumably the #2 clinical role at Allakos after his father's, making the nepotism even more troubling. The proxy filed on Apr 30, 2019 says his title is Director, so either the disclosure was incorrect or he's been promoted.

Warning sign #4 (cont'd): Flagrant nepotism in key clinical roles

The main purpose of a clinical-stage biotech company is running clinical trials, giving these roles outsized importance - and sway, given their father's authority as a C-level officer - particularly at a company with so few employees: a mere 77 total employees as of late Nov 2019 and only 46 at the time of the S-1.

Investors should be asking, are these the most qualified candidates Allakos can find given the Q3 cash balance of $517mm, and the substantial institutional capital raised prior to IPO? We intend no disrespect to Ms. Shaw, but find her significantly underqualified for the position and question why the company has structured its clinical trials organization in this manner. We can locate no work history online for Jacob Rasmussen, which we find unusual for a role this senior.

Running clinical trials at an early stage biotech is a high-risk endeavor with little margin for error. The stakes are high. We wonder why a first-time Clinical Program Manager, with a bio that suggests a succession of junior roles, is entrusted with these responsibilities, and are curious as to the qualifications that led to the son (we believe) to be the VP of Clinical Operations.

We also wonder why the daughter appears to be the only employee based in Utah, and why the father and son are based in Maryland, when almost every Allakos employee on LinkedIn appears to be based at the HQ in the San Francisco Bay Area. We find it unusual that the pivotal, core function of Allakos appears to be handled remotely by a nepotistic triangle.

Warning sign #4: Flagrant nepotism in key clinical roles

We note the level of compensation afforded to the CMO's children. In 2017/18, Jacob Rasmussen was awarded stock options to purchase ~65k shares and Camilla Shaw ~35k shares – a total of 100k shares with a gross value of ~$13mm at the recent ALLK price of $130/share.

Allakos S-1 filed July 17, 2018

Transactions with Certain Employees

Our current Director of Clinical Project Management, Jacob Rasmussen and our current Clinical Program Manager, Camilla Shaw, are the son and daughter of Dr. Henrik Rasmussen, our Chief Medical Officer. Mr. Jacob Rasmussen and Ms. Shaw receive an annual salary of $140,000 and $150,000, respectively, and certain benefits that are also provided to our other similarly situated employees, which benefits have an approximate annual value of $23,000 to each of Mr. Jacob Rasmussen and Ms. Shaw. During the fiscal year ended December 31, 2017, Mr. Jacob Rasmussen and Ms. Shaw were also awarded discretionary cash bonuses in the amount of approximately $15,000 and $6,000, respectively, and stock options to purchase up to 48,000 and 16,800, respectively, shares of our common stock, subject to vesting. On May 15, 2018, Mr. Jacob Rasmussen and Ms. Shaw were awarded additional stock options to purchase up to 11,120 and 13,040, respectively, shares of common stock, subject to vesting. Prior to her employment as Clinical Program Manager, Ms. Shaw provided services to us as a consultant from July 2017 to September 2017, during which time she received approximately $36,000 in cash compensation for services provided.

Allakos proxy statement filed April 30, 2019

Transactions with Certain Employees

Our current Director of Clinical Project Management, Jacob Rasmussen, and our current Clinical Program Manager, Camilla Shaw, are the son and daughter of Dr. Henrik Rasmussen, our Chief Medical Officer. Mr. Jacob Rasmussen and Ms. Shaw receive an annual salary of $161,000 and $150,000, respectively, and certain benefits that are also provided to our other similarly situated employees, which benefits have an approximate annual value to Mr. Jacob Rasmussen and Ms. Shaw of $38,000 and $30,000, respectively. During the fiscal year ended December 31, 2018, Mr. Jacob Rasmussen and Ms. Shaw were also awarded discretionary cash bonuses in the amount of approximately $32,000 and $23,000, respectively, and stock options to purchase up to 17,320 and 18,140, respectively, shares of our common stock, subject to vesting

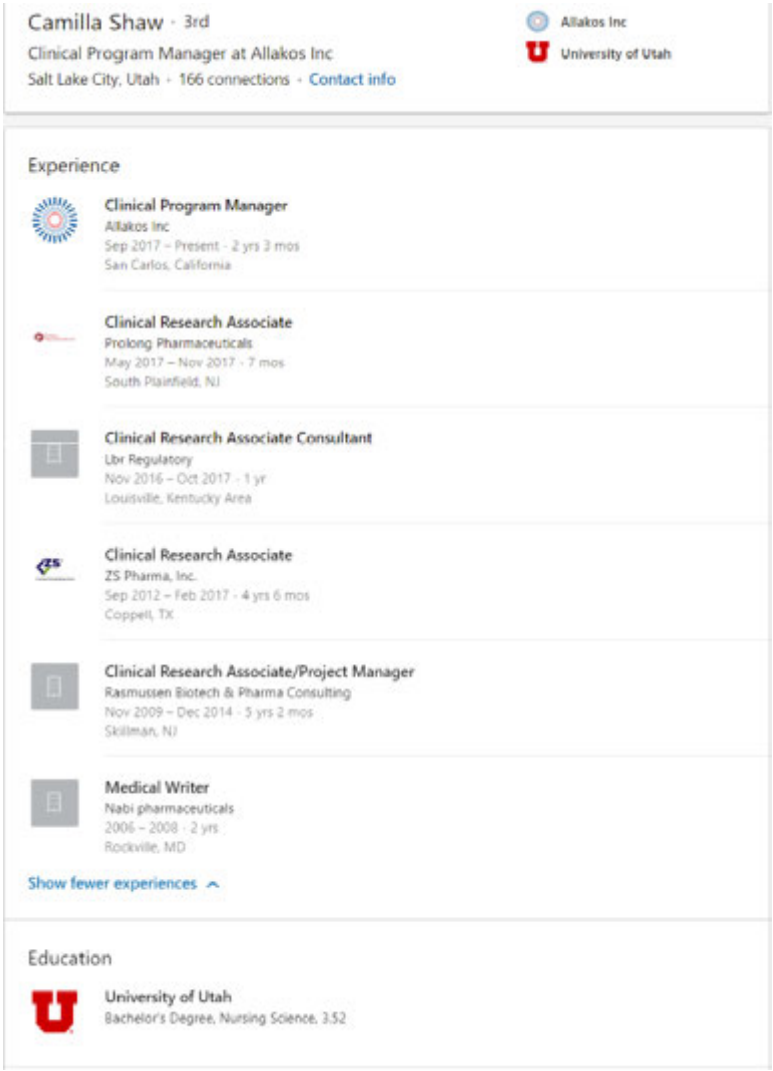
Source: SEC filings

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

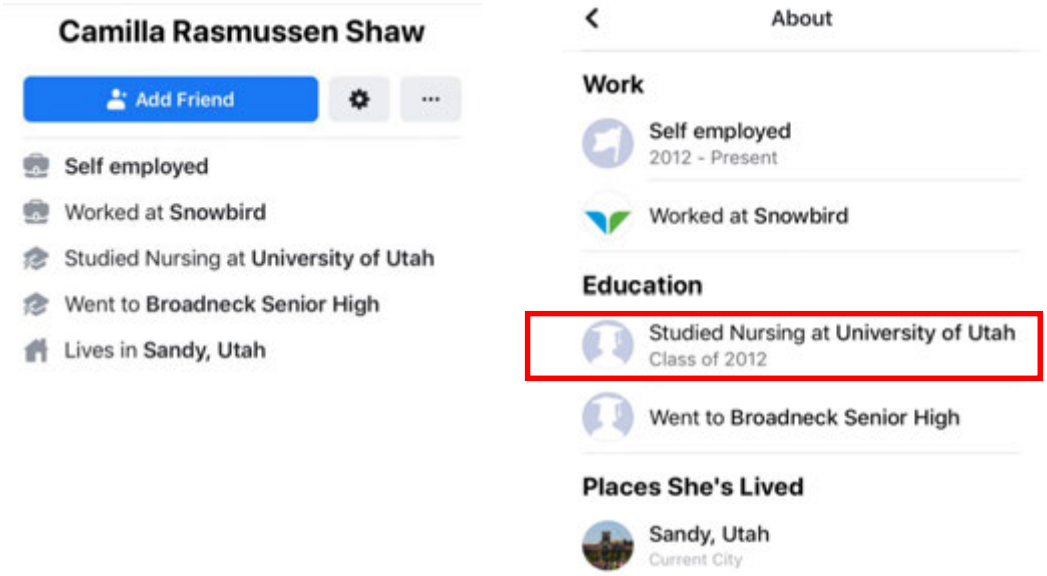
Warning sign #4: Flagrant nepotism in key clinical roles

Ms. Shaw's LinkedIn bio indicates that this is her first role as "Clinical Program Manager." Prior roles in our opinion were extremely junior. The bio doesn't provide a timeframe for college but her public Facebook profile says 'Class of 2012."

LinkedIn profile



Public Facebook profile pages



Source: https://www.facebook.com/camilla.rasmussenshaw; red ours for emphasis.

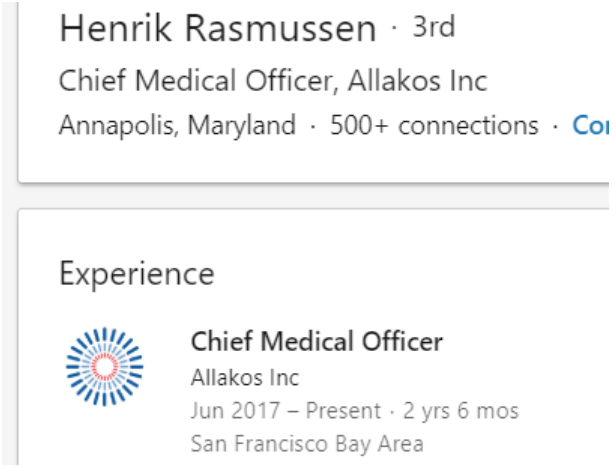
Source: https://www.linkedin.com/in/camilla-shaw-60505689/

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

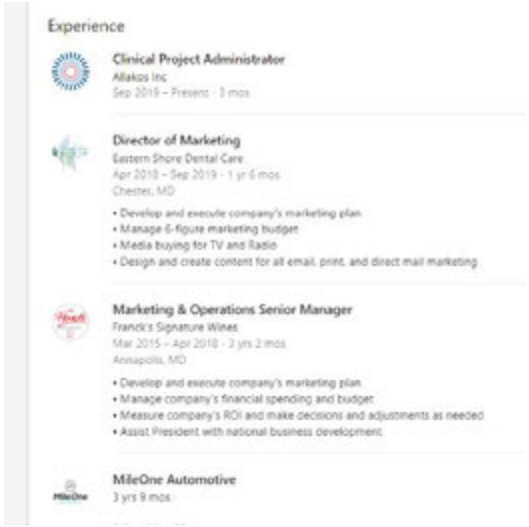
Warning sign #4: Flagrant nepotism in key clinical roles

We note another concerning aspect of the Rasmussen family's involvement with Allakos. Of the 77 employees listed on LinkedIn as of late Nov 2019, almost all are based in the San Francisco Bay Area. We found no other office in the 10K or the website except the HQ in Redwood City, CA. Therefore, we wonder why the CMO's daughter is the only Allakos employee based in Utah, and how a first-time Clinical Program Manager is afforded such autonomy. As another red flag, the CMO's LinkedIn bio indicates suggests he's based in Maryland. Only two other Allakos bios state Maryland as the location. The first is the Clinical Project Administrator – whose last three employers were Eastern Shore Dental Care, Franck's Signature Wines, and MileOne Automotive.

CMO LinkedIn bio says he's based in Maryland



Clinical Project Administrator is one of two other employees in MD



Source: https://www.linkedin.com/in/henrik-rasmussen-ba34b115/; https://www.linkedin.com/in/katiemazz/

Warning sign #4: Flagrant nepotism in key clinical roles

The other is for a VP Clinical Operations. The LinkedIn bio is privacy-restricted but we believe the bio is for the CMO's son, Jacob Rasmussen, based on an interview the CMO gave to a local paper. The April 2019 proxy statement says Jacob Rasmussen was the Director of Clinical Project Management. Either that disclosure is incorrect, or he has been promoted to VP – which sounds to us like the #2 clinical role at Allakos after his father – which if true would make the nepotism even more serious. We find it troubling that almost every LinkedIn bio for Allakos states the location as the Bay Area, yet the most critical function appears to be handled remotely by nepotistic triangle. Moreover, we find it unusual that we can find nothing online about Jacob Rasmussen's professional history, given the length of experience required for a role this senior.

LinkedIn Member

Vice President Clinical Operations at Allakos, Inc

Baltimore, Maryland Area

"We liked and missed Annapolis," said Henrik*. "When I started my own company, Rasmussen Biotech & Pharma Consulting, LLC, we moved back to Annapolis in 2012."* ***Their three children are grown and have, almost, flown the coop […] An Annapolis resident, Jacob is 31 and director of project management for a biotech company.*** *– Interview with local paper, 2014*

Source: LinkedIn search results for the search term "Allakos"; https://www.capitalgazette.com/education/naval-academy/cg2-arc-140208cc-home-of-the-week-20140208-story.html

Warning sign #5: Poor controls as well as Allakos' role in running the study itself rendered the ENIGMA trial – purportedly randomized and double-blind - essentially unblinded, making the already subjective endpoint of patient-reported symptom scores a sham. The FDA has cautioned that "Suspicion of inadvertent unblinding can be a problematic review consideration for the FDA when assessing PRO endpoints." Shockingly, a parent posted about speaking to Allakos - the co-founder plus what we infer to be contact with the CMO - which if true would strike us as reckless and raise concerns about trial tampering and Allakos' conduct in general.

Numerous posts by trial participants on Facebook, as well as expert consultations with six investigators from the trial, lead us to conclude that PRO scores were plagued by bias and unreliability. One trial participant even posted that *"being able to see the test results, biopsies, bloodwork while on the drug was so great."*

The veracity of blinding is a crucial issue for investors to assess, as their euphoria currently rests on little more than a small n trial with risks similar to those of open-label trials. We believe investors are oblivious to a disastrous scenario is phase 3, as the FDA has specifically cautioned about blinding controls in the context of PRO endpoints: *"Suspicion of inadvertent unblinding can be a problematic review consideration for the FDA when assessing PRO endpoints….The effect of intentional unblinding is important to consider in the interpretation of clinical trial results."*

Trial investigators stated that Allakos ran the study itself vs. through a CRO. We wonder how a trial is blinded is the sponsor is intimately involved with trial sites and knows which patients are on drug or placebo. A parent of a trial participant posted on Facebook that she spoke with

Warning sign #5 (cont'd): Poor controls as well as Allakos' role in running the study itself rendered the ENIGMA trial – purportedly randomized and double-blind - essentially unblinded

an Allakos co-founder and member of its scientific advisory board, and her post appears to suggest that she also spoke with the Chief Medical Officer. This strikes us as reckless and makes a farce of a "blinded" trial, and raises concerns about tampering and Allakos' conduct in general.

If patients and/or their doctors know or strongly believe that they're receiving the drug, the potential for junk PRO results is self-evident, given the subjective nature of patients self-reporting scores, magnified by the despondent and suggestible nature of participants as evidenced by Facebook posts.

1. **Concerns around blinding and bias are shared by Allakos trial investigators that we consulted, who indicated that infusion-related reactions may have unblinded the trial. These concerns are corroborated by a large volume of patient posts online.**

2. **Posts indicate that patients received ongoing endoscopies during the trial, with feedback from trial investigators about visual improvement or worsening of the stomach and esophagus. The volume of posts indicate massive blinding problems from doctors using endoscopy results to tell patients whether they are most likely on AK002 or placebo. One post stated that "*clinically and by endoscopy we all should have a clear indication if we are getting the drug or placebo.*"**

Warning sign #5 (cont'd): Poor controls as well as Allakos' role in running the study itself rendered the ENIGMA trial – purportedly randomized and double-blind - essentially unblinded

3. **A trial investigator we consulted spoke about running CBC (complete blood count) panels during the trial to measure eosinophils for "curiosity," further magnifying the blinding problems created by endoscopies. Another investigator stated that patients could easily get CBC scans themselves at any clinic. Facebook posts suggest that patients were sophisticated and motivated in trying to determine if they were on AK002, given the overnight travel and other inconveniences that some of them detailed.**

4. **A high volume of Facebook posts indicate that patients had strong opinions about whether they were on drug or placebo, whether correct or incorrect irrespective of endoscopic or CBC panel feedback. While this may be an issue in any trial, the nature and volume of patient posts suggests a particularly extreme dynamic at play.**

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #5: Poor controls rendered the trial essentially unblinded

Three separate ENIGMA investigators indicated concerns around the veracity of the trial's blinding. Two are prominent KOL's in the space. Investigators indicated that the occurrence of adverse effects could easily have unblinded patients as to whether they were on drug, versus placebo. They also indicated that patients could easily get an eosinophil count themselves in a standard blood panel, and indicated further unblinding via ongoing endoscopies during the trial.

"The infusion reactions could unblind you." ***– ENIGMA investigator and KOL***

"You could argue that from a symptom standpoint, the trial was unblinded*. If you have a reaction, you say as a patient that I can't be on placebo.* ***Absolutely, that's a confounder factor****. It's one of the things you have to worry about. Patients think if I'm on placebo, I won't respond."* ***- Another ENIGMA investigator***

*"****Unblinding through infusion is certainly a possibility, of a confounding factor****. A lot of times people think they're on a drug.* ***If someone needs IV resuscitation after the drug goes in, the staff would say the patient is on the drug."*** ***– Third ENIGMA investigator and KOL***

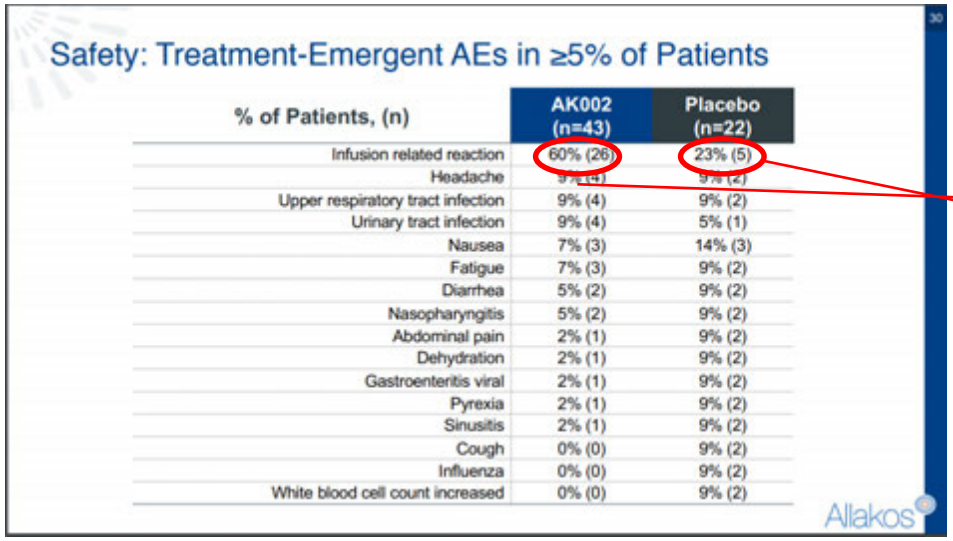
"A patient can go to a hospital and get a CBC, complete blood count for eosinophils. *It's something that could have happened. You can find out if you're curious.* ***This used to be a big concern in trials."*** ***– Third ENIGMA investigator and KOL***

"When doing endoscopy, the doctor is not blinded to visual findings. He may say it looks like you're getting better. That doctor should be blinded*. But patient can get a CBC panel themselves."* ***– Third ENIGMA investigator and KOL***

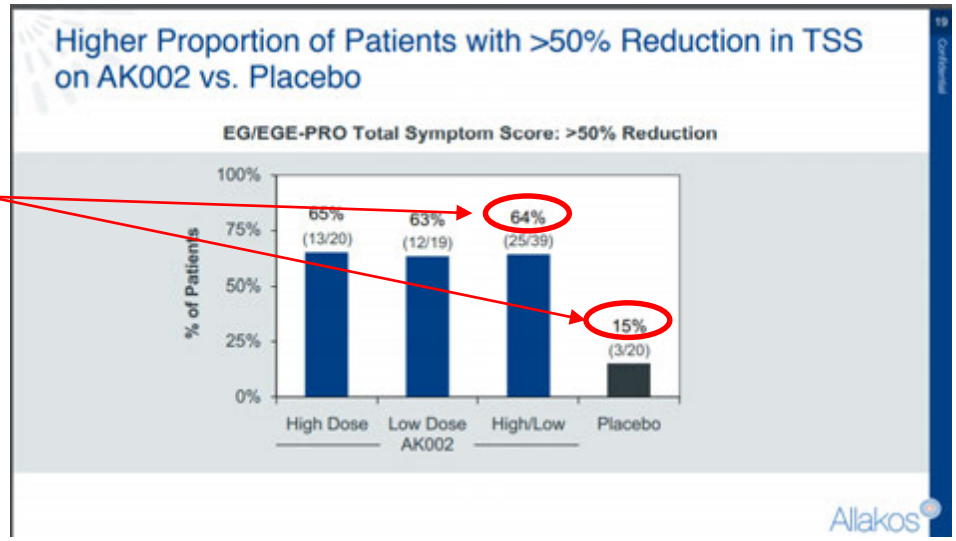
Source: Seligman expert consultations

Warning sign #5: Poor controls rendered the trial essentially unblinded

***We note a striking feature of the ENIGMA data:* the infusion reaction rates in the AK002 arm (60%) vs placebo (23%) are very similar to the patient-reported symptom score response rates for AK002 (64%) vs placebo (15%). *We see no explanation for this similarity except that infusion reactions unblinded patients and were the driver of symptom scores*. In other words, 60% of patients had an infusion reaction and logically concluded they were on AK002, leading to about the same percentage of patients reporting symptom improvement.**



% of Patients, (n)	AK002 (n=43)	Placebo (n=22)
Infusion related reaction	60% (26)	23% (5)
Headache	9% (4)	9% (2)
Upper respiratory tract infection	9% (4)	9% (2)
Urinary tract infection	9% (4)	5% (1)
Nausea	7% (3)	14% (3)
Fatigue	7% (3)	9% (2)
Diarrhea	5% (2)	9% (2)
Nasopharyngitis	5% (2)	9% (2)
Abdominal pain	2% (1)	9% (2)
Dehydration	2% (1)	9% (2)
Gastroenteritis viral	2% (1)	9% (2)
Pyrexia	2% (1)	9% (2)
Sinusitis	2% (1)	9% (2)
Cough	0% (0)	9% (2)
Influenza	0% (0)	9% (2)
White blood cell count increased	0% (0)	9% (2)



Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #5: Poor controls rendered the trial essentially unblinded

Poor blinding controls are a massive red flag which the FDA has specifically cautioned about in its guidance document for symptom improvements measured with a PRO (patient-reported outcome) instrument. The FDA calls out unblinding from adverse effects, and warns that "suspicion of inadvertent unblinding can be a problematic review consideration for the FDA when assessing PRO endpoints."

"Patients who know they are in an active treatment group may overestimate benefit *whereas patients who know they are not receiving active treatment may underreport any improvement actually experienced."*

"In blinded clinical trials, patients should be blinded to treatment assignment throughout the trial. ***If the treatment has obvious effects, such as adverse events, the clinical trial may be at risk for unintentional unblinding."***

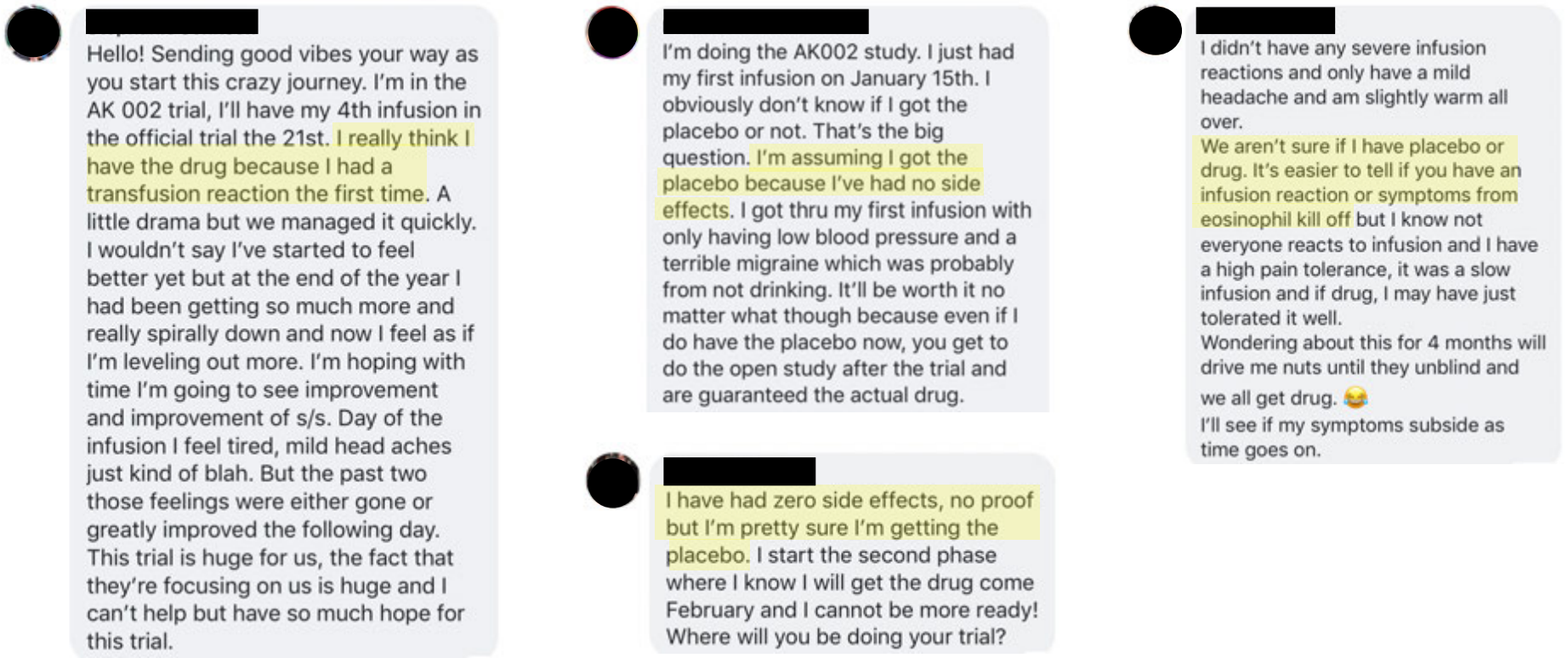
"Suspicion of inadvertent unblinding can be a problematic review consideration for the FDA when assessing PRO endpoints."

"The effect of intentional unblinding is important to consider in the interpretation of clinical trial results."

Source: https://www.fda.gov/media/77832/download

Warning sign #5: Poor controls rendered the trial essentially unblinded

Patients in the trial actively posted about their experiences on a Facebook group for eosinophilic gastritis, often in real-time during infusions. The group lists over 1,000 members, with hundreds of posts by trial participants or their families. We suspect that most, if not the vast majority of the 65 participants in the Allakos trial may be members of the group. The patients and/or their families strike us as sophisticated, knowledgeable, and well-read about the condition – creating a unique and problematic echo chamber for this trial. Patients clearly associated infusion-related reactions or other side effects with being on the drug, as evidenced by four different patients below.

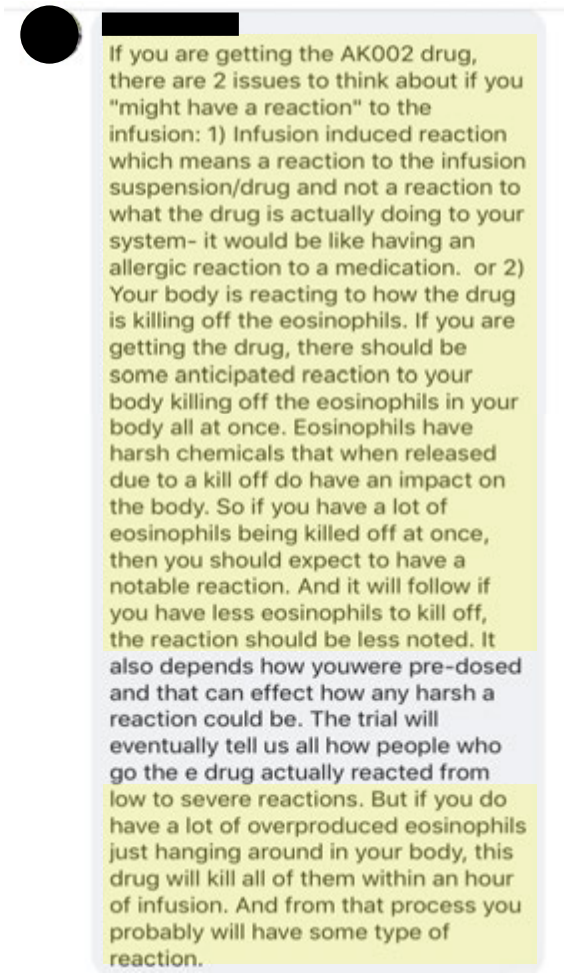


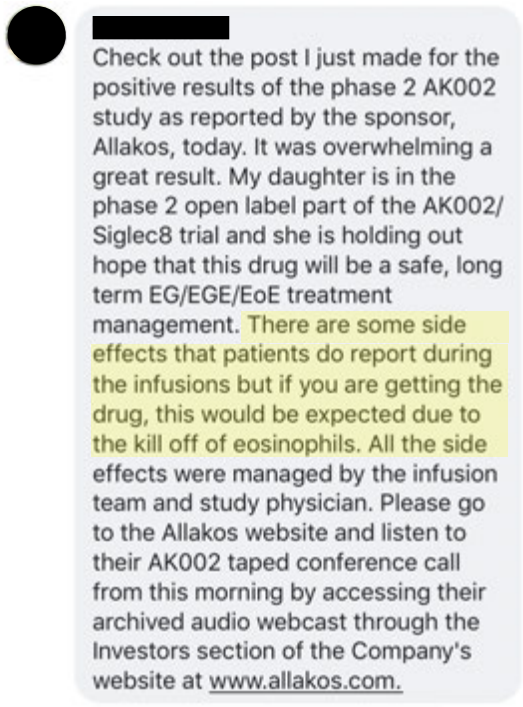
Source: https://www.facebook.com/groups/258285487951166/

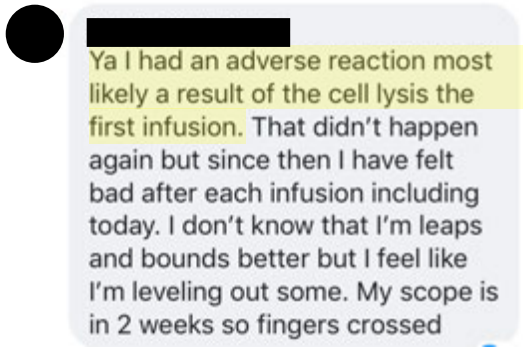
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

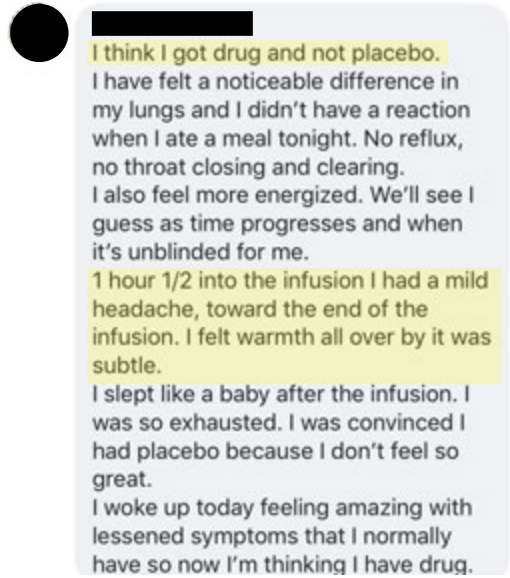
Warning sign #5: Poor controls rendered the trial essentially unblinded

Aside from the infusion itself, patients posted that eosinophil depletion triggered side effects and was further indication that they were getting AK002.







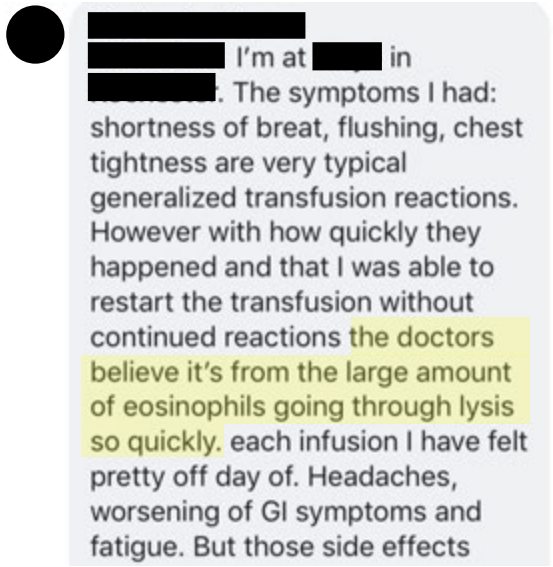


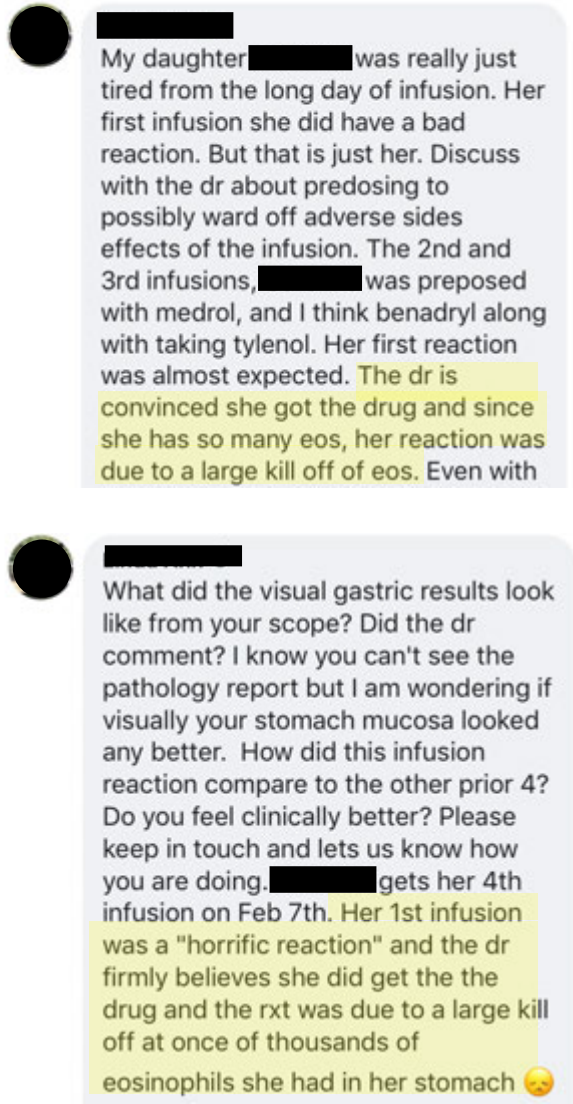
Source: https://www.facebook.com/groups/258285487951166/

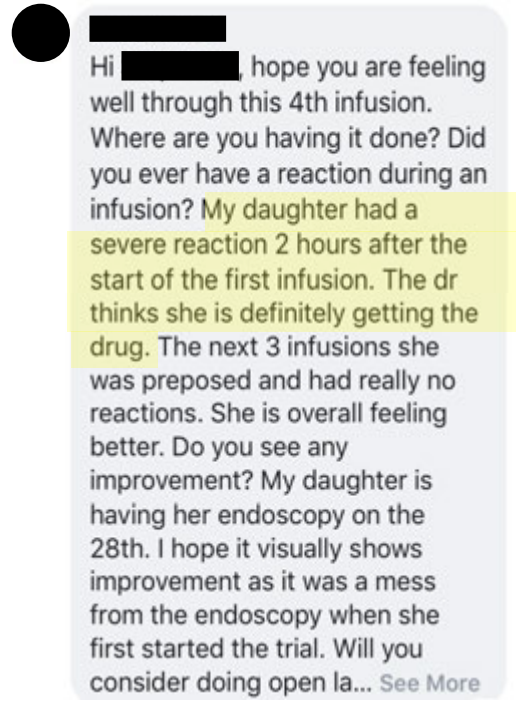
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #5: Poor controls rendered the trial essentially unblinded

Trial investigators compounded patients' own associations between reactions and being in the active arms. Given doctors' influence, the suggestibility and bias in patient-reported symptom scores is self-evident.





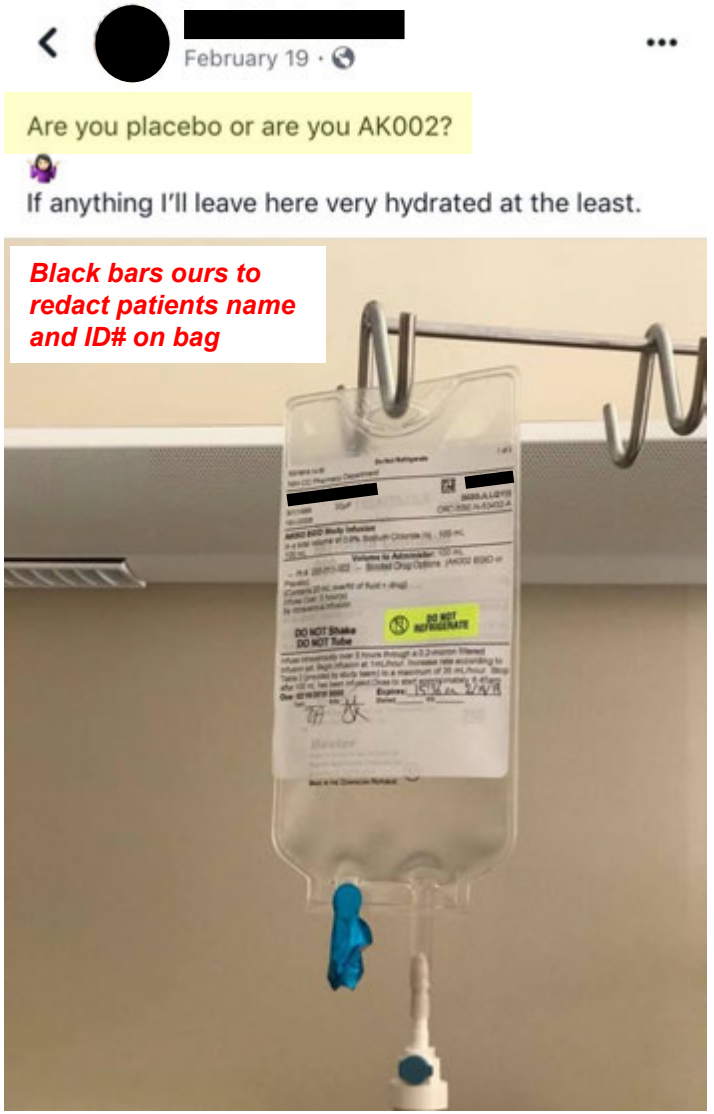


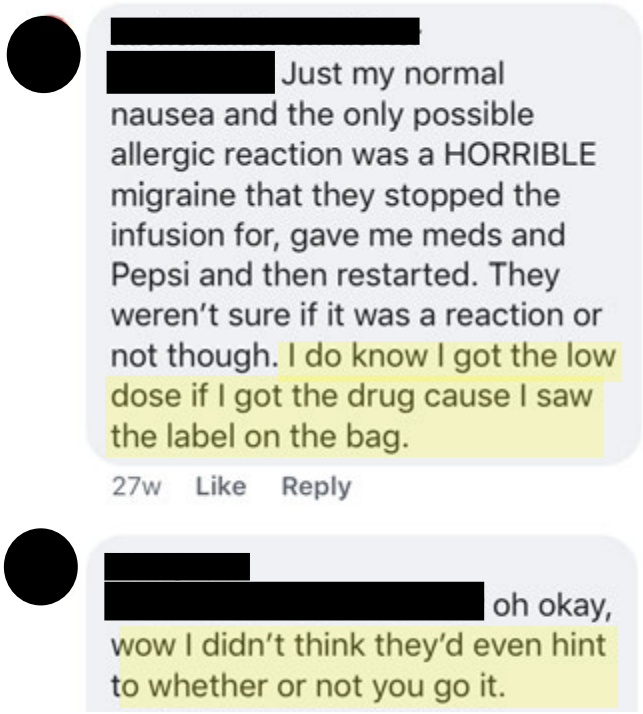
Source: https://www.facebook.com/groups/258285487951166/

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #5: Poor controls rendered the trial essentially unblinded

Patients scrutinized and posted pictures or comments about their IV packs, and conveyed strong beliefs about whether they were on low or high dose based on the labels. One patient remarked "wow I didn't think they'd even hint to whether or not you go[t] it."

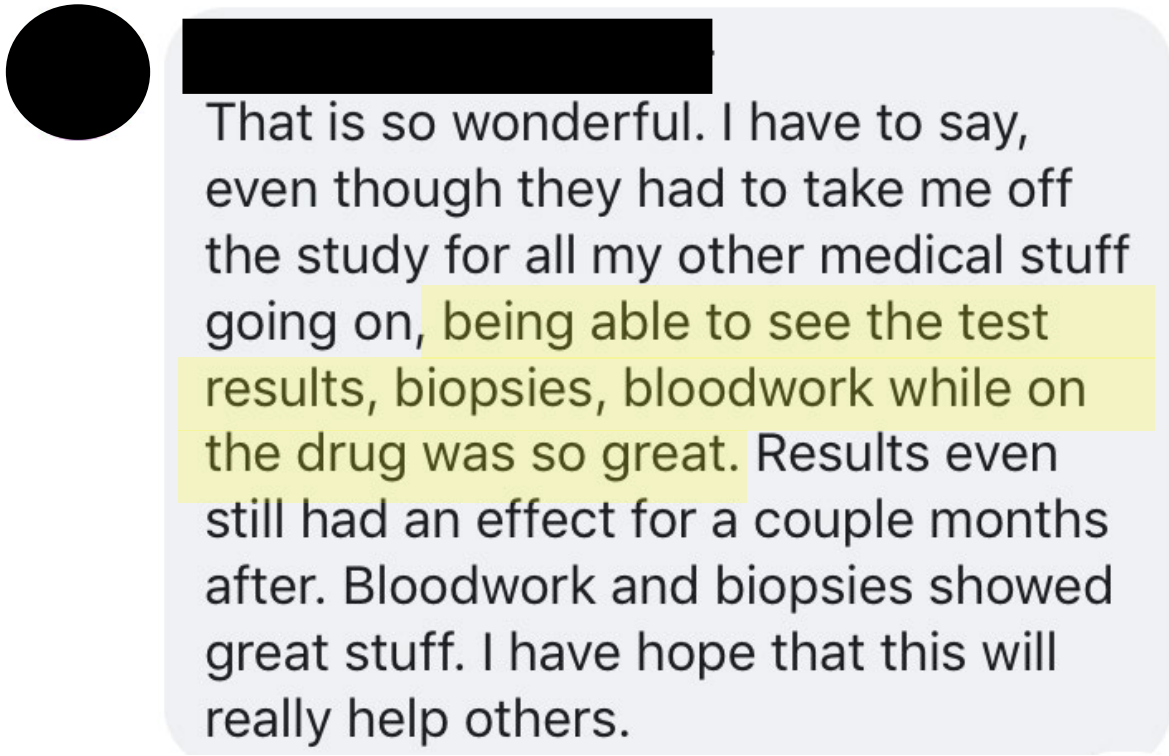




Source: https://www.facebook.com/groups/258285487951166/

Warning sign #5: Poor controls rendered the trial essentially unblinded

Shockingly, one patient reported having access to 'test results, biopsies, bloodwork while on the drug."



Source: https://www.facebook.com/groups/258285487951166/

Warning sign #5: Poor controls rendered the trial essentially unblinded

Patients reported receiving ongoing endoscopy results during the trial (referred to as EGD - "esophagogastroduodenscopy"), and their doctors correlated visual improvement or worsening with being on AK002 or placebo, respectively. One person went so far as to state that "clinically and by endoscopy we all should have a clear indication if we are getting the drug or placebo."

[redacted] Ok that all sounds like a good plan. The dr also thinks that [redacted] is getting the drug but won't have her endoscopy until 2/28. So we are really not sure until she sees her gastric tissue for hopefully some healing. [redacted] did have that

[redacted] Yes, thanks, and of course I still have hope. I just felt slapped down yesterday with the realization that [redacted] does have EG clinical signs active EG. I haven't felt that way like I did yesterday in a long time, and it just took me all by surprise. I am usually positive as far as "HOPE" especially with the AK002 trial drug showing some improvement with her latest scope. I just want it to be over and

[redacted] ▸ Eosinophilic Gastritis Support Group
February 28 ·

At [redacted] ~ [redacted] is having her follow up endoscopy for the AK002 drug study 👍Great news! Doctor says everything looks better in her throat n stomach🎉💞👍😍 We are so happy 🙏 Prayers answered 😍

[redacted] What did the visual gastric results look like from your scope? Did the dr comment? I know you can't see the pathology report but I am wondering if visually your stomach mucosa looked any better. How did this infusion

[redacted] Ya I had an adverse reaction most likely a result of the cell lysis the first infusion. That didn't happen again but since then I have felt bad after each infusion including today. I don't know that I'm leaps and bounds better but I feel like I'm leveling out some. My scope is in 2 weeks so fingers crossed

[redacted] I am participating and am now in the open label phase. I am sure I got drug the first round because I saw improvement on my follow up EGD. I had minimal side effects. Just some burning skin almost like a sunburn and headache. First dose of med in open label, with same side effects. Haven't seen a whole lot of symptom improvement though so hoping that will come with more healing of my ulcers and inflammation.

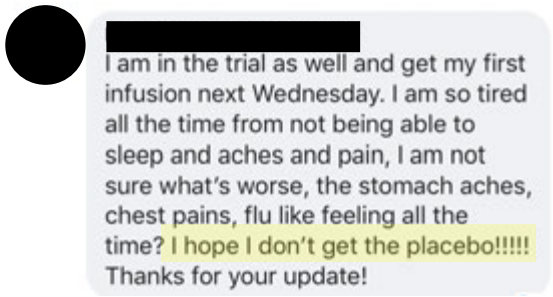
[redacted] [redacted] so happy you are finished with the infusions. How did you do? Do you feel any better clinically. It's funny you ask that question. I asked the research assistant yesterday who explains everything to us that exact question and she said yes, you do find out in the open label part.... and then I asked the doctor (who was reluctant to discuss this with me because she said her research assistant answers all these questions) and she said no, we all don't find out until the study has ended. So I believe the doctor. I would think if you are getting the drug and it is not helping based on blood work and pathology biopsy, then the study would have to disclose to you that you are not eligible to continue with the drug in the open label part of the study. So I agree with you we all don't find out until the study is over. But clinically and by endoscopy we all should have a clear indication if we are getting the drug or placebo. At this point I am just

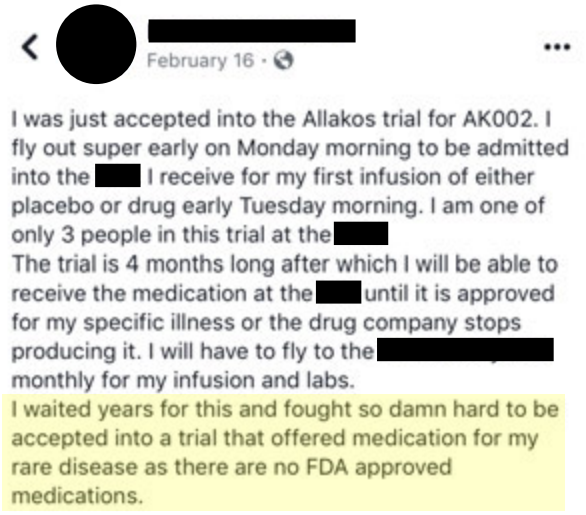
Source: https://www.facebook.com/groups/258285487951166/

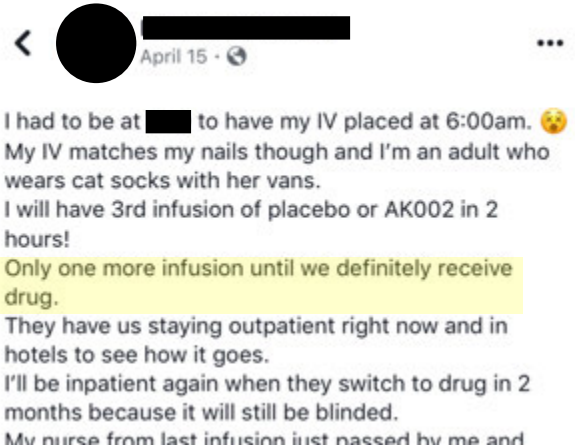
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

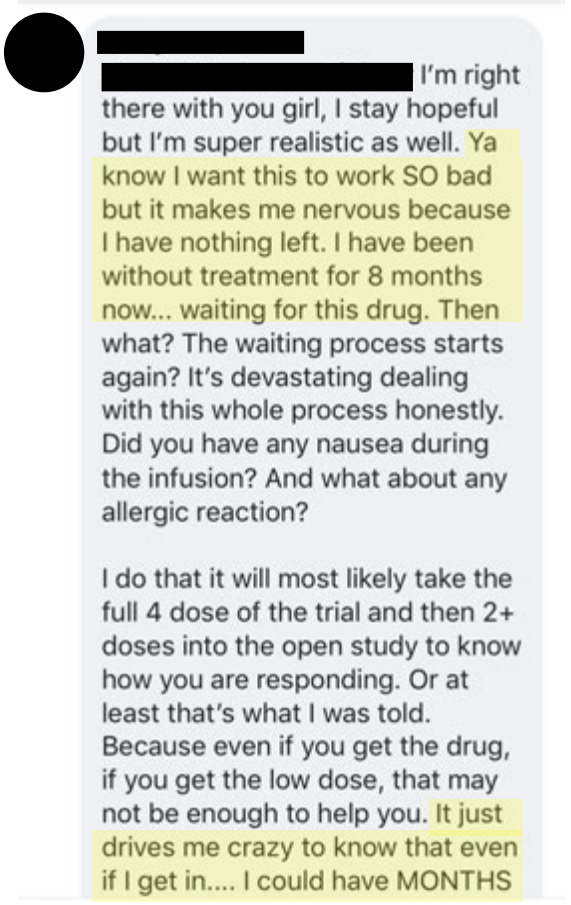
Warning sign #5: Poor controls rendered the trial essentially unblinded

Posts suggest that trial participants were extremely motivated to be accepted into the extension study where all patients would receive the drug and avoid placebo, and that they would be allowed to continue only if they had "success" in the ENIGMA trial, potentially creating a perverse incentive for them to report symptom improvements on the PRO scale.









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Seligman Investments | ALLAKOS (NASDAQ: ALLK)

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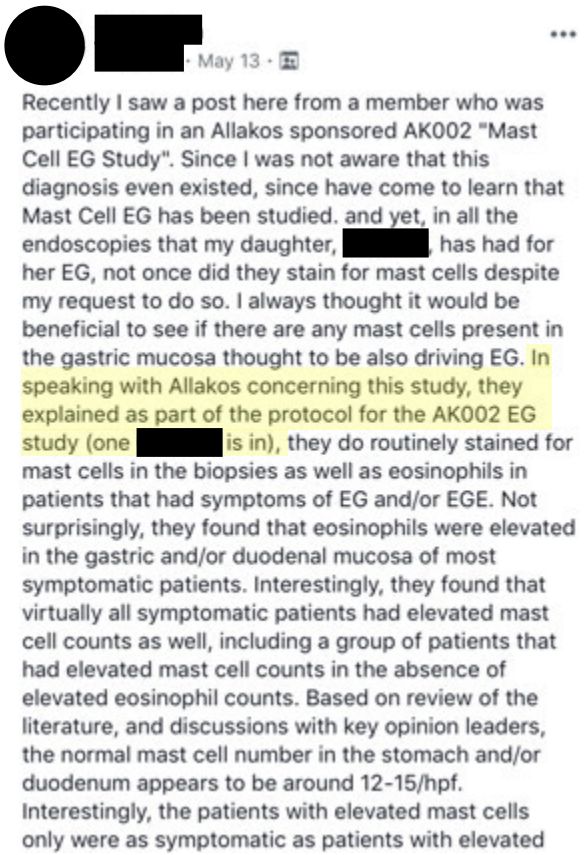
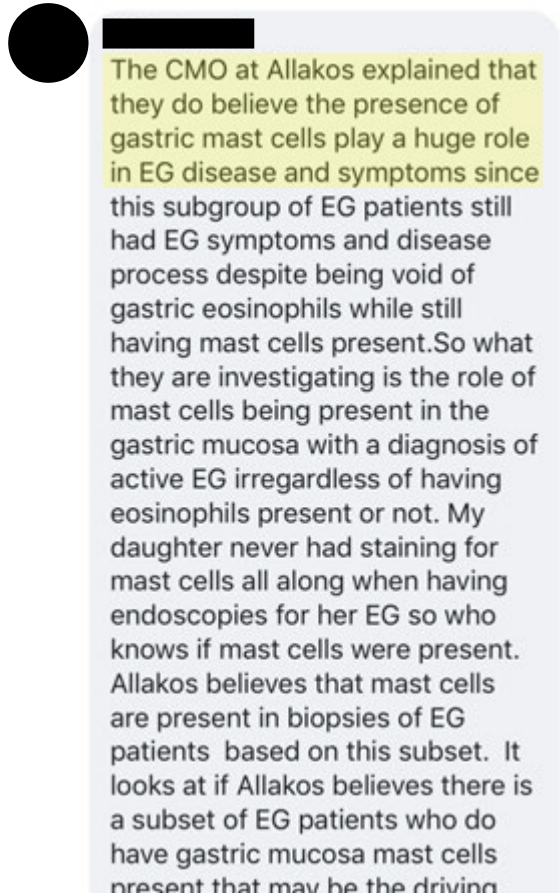
The parent of a trial participant reported speaking with Allakos, specifically mentioning the company's co-founder and a member of its scientific advisory board, as well as what we infer to be communication with the Chief Medical Officer. The communication – if true – would strike us as reckless and would make a farce of a "blinded" trial, and raise concerns about tampering and Allakos' conduct in general.



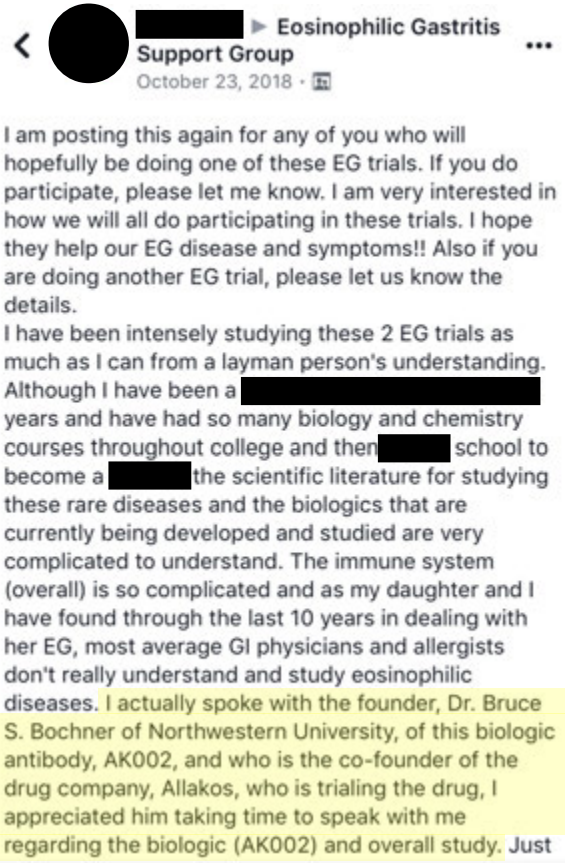
[redacted] · May 13 ·

Recently I saw a post here from a member who was participating in an Allakos sponsored AK002 "Mast Cell EG Study". Since I was not aware that this diagnosis even existed, since have come to learn that Mast Cell EG has been studied. and yet, in all the endoscopies that my daughter, [redacted], has had for her EG, not once did they stain for mast cells despite my request to do so. I always thought it would be beneficial to see if there are any mast cells present in the gastric mucosa thought to be also driving EG. In speaking with Allakos concerning this study, they explained as part of the protocol for the AK002 EG study (one [redacted] is in), they do routinely stained for mast cells in the biopsies as well as eosinophils in patients that had symptoms of EG and/or EGE. Not surprisingly, they found that eosinophils were elevated in the gastric and/or duodenal mucosa of most symptomatic patients. Interestingly, they found that virtually all symptomatic patients had elevated mast cell counts as well, including a group of patients that had elevated mast cell counts in the absence of elevated eosinophil counts. Based on review of the literature, and discussions with key opinion leaders, the normal mast cell number in the stomach and/or duodenum appears to be around 12-15/hpf. Interestingly, the patients with elevated mast cells only were as symptomatic as patients with elevated



[redacted]

The CMO at Allakos explained that they do believe the presence of gastric mast cells play a huge role in EG disease and symptoms since this subgroup of EG patients still had EG symptoms and disease process despite being void of gastric eosinophils while still having mast cells present.So what they are investigating is the role of mast cells being present in the gastric mucosa with a diagnosis of active EG irregardless of having eosinophils present or not. My daughter never had staining for mast cells all along when having endoscopies for her EG so who knows if mast cells were present. Allakos believes that mast cells are present in biopsies of EG patients based on this subset. It looks at if Allakos believes there is a subset of EG patients who do have gastric mucosa mast cells present that may be the driving



[redacted] ▶ Eosinophilic Gastritis Support Group

October 23, 2018 ·

I am posting this again for any of you who will hopefully be doing one of these EG trials. If you do participate, please let me know. I am very interested in how we will all do participating in these trials. I hope they help our EG disease and symptoms!! Also if you are doing another EG trial, please let us know the details.

I have been intensely studying these 2 EG trials as much as I can from a layman person's understanding. Although I have been a [redacted] years and have had so many biology and chemistry courses throughout college and then [redacted] school to become a [redacted] the scientific literature for studying these rare diseases and the biologics that are currently being developed and studied are very complicated to understand. The immune system (overall) is so complicated and as my daughter and I have found through the last 10 years in dealing with her EG, most average GI physicians and allergists don't really understand and study eosinophilic diseases. I actually spoke with the founder, Dr. Bruce S. Bochner of Northwestern University, of this biologic antibody, AK002, and who is the co-founder of the drug company, Allakos, who is trialing the drug, I appreciated him taking time to speak with me regarding the biologic (AK002) and overall study. Just

Source: https://www.facebook.com/groups/258285487951166/

Warning sign #5: Poor controls rendered the trial essentially unblinded

An Allakos ENIGMA Trial Investigator - a prominent physician and KOL in the space - expressed concern at this possibility, calling it "weird" and "unusual" in the context of a blinded trial.

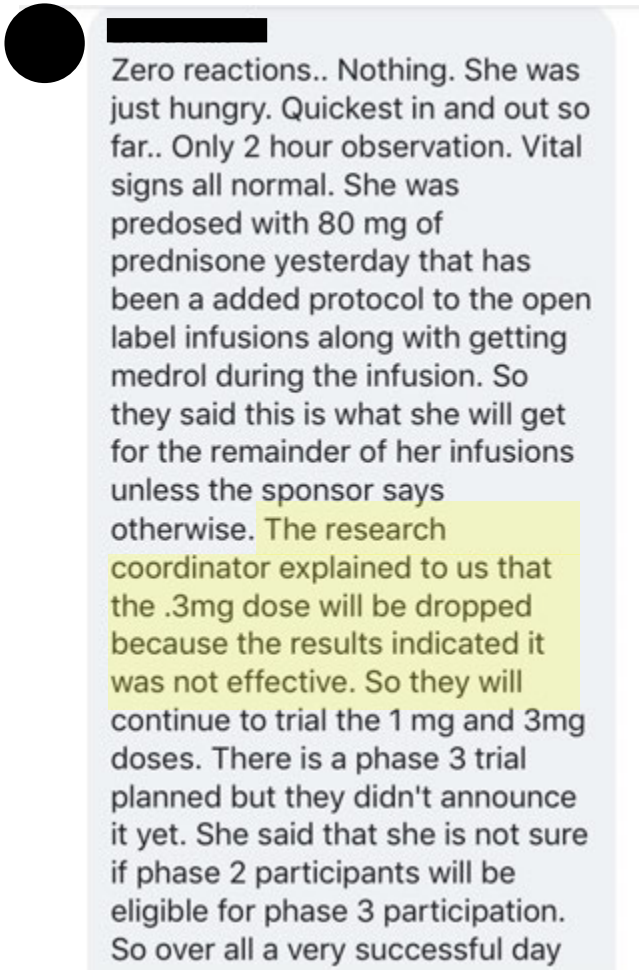
"If Rasmussen [Allakos Chief Medical Officer] talked to a patient's parent, that's what I mean when I say they were heavily involved. That's unusual. It seems a little weird to me. The company should be blinded to the patient's name. It doesn't make any sense*. The patient's ID is a private matter. Patients are desperate. Parents sometimes call the company. It's a gray area. Once a patient identifies themselves to the company, it's a HIPAA violation. It's concerning to some degree.* ***He could be influencing them. Randomization should be done by investigational pharmacist at each site. It's unusual and is a little concerning."***

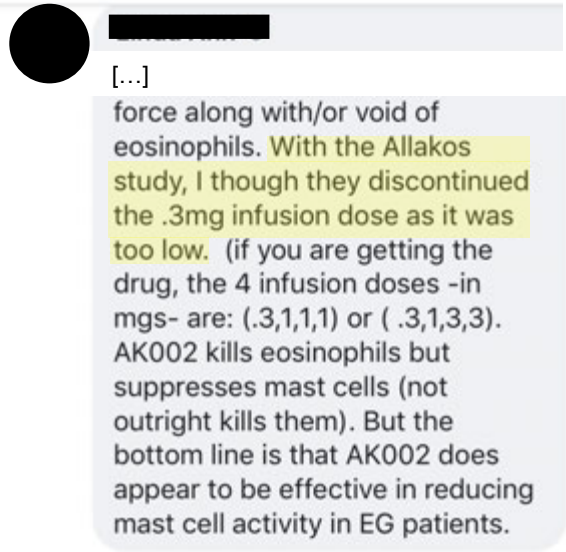
– Allakos ENIGMA Phase 2 Trial Investigator and a prominent physician/KOL in the space

Source: Seligman expert consultations

Warning sign #5: Poor controls rendered the trial essentially unblinded

A post from April 2019 mentions a research coordinator disclosing that "the .3mg dose will be dropped because the results indicated it was not effective. So they will continue to trial the 1mg and 3mg doses." If Allakos had unfettered access to patient data and results well before the end of the trial and a research coordinator – we presume at a trial site – was able to prematurely speak to study "results," then we wonder how the trial can be described at "blinded."





Source: https://www.facebook.com/groups/258285487951166/

Warning sign #6: What appears to be a last minute, unexplained expansion of the ENIGMA trial, with insufficient time for new patients to complete the study's pre-specified protocol, then followed by the exclusion of patients for a cherry-picked "Per Protocol" group around which the topline results are framed – a curious scenario given Allakos' role in running the study, nepotism, unblinding – and as we detail later, the role of one or two patients in barely pushing the study into statistical significance, despite n=65, according to a number of biostatisticians we consulted, including two known for identifying discrepancies or fraud in clinical trials.

Allakos' phase 2 trial results presentation and call on August 5, 2019 indicated that 65 patients participated in the trial. However, as of January 4th, 2019, the ClinicalTrials.gov page for the ENIGMA trial still indicated a total of 60 patients.

Companies typically disclose trial size expansions, but we can find no such disclosure by Allakos prior to the final trial results, even at its Investor Day on February 19, 2019, where it again stated that the trial was powered with 60 patients. We note that the analyst day occurred deep into the trial and only a few months before it ended.

This is problematic as patients enrolled after February/March lacked time to complete the pre-specified protocol by the study's June 24th completion date. Even if the new patients were magically added on February 20th - implausible given the rarity of EG/EGE and difficulty in finding participants) – following the protocol would have pushed them into September, by our calculation, and corroborated by color from trial investigators on the study's duration.

Warning sign #6 (cont'd): What appears to be a last minute, unexplained expansion of the ENIGMA trial, with insufficient time for new patients to complete the study's pre-specified protocol

Mid-trial study adjustments - 11th hour in this case - which expand the sample size and powering are a red flag, as they suggest that the study is failing to show statistical significance. Companies try to salvage the study by enrolling more subjects in the hope that a larger N will capture a smaller effect. We have historically found such modifications to be predictive of trial failure, with shares often declining upon these disclosures. Common sense indicates that if a study is pointing to efficacy, a public company has little incentive to expand the sample size and rock the boat.

The sequence is troubling: Allakos likely had real-time data as they ran the study themselves; then appear to have quietly expanded the trial size; new patients lacked time to complete the pre-specified protocol; patients were then excluded to cherry-pick a Per Protocol group; and the trial appears to have barely scraped over the finish line with one or two patients driving statistical significance, as we detail in a later section.

Warning sign #6: The unexplained, last minute expansion of the ENIGMA trial

Allakos' phase 2 trial results presentation and call on August 5, 2019 indicated that 65 patients participated in the trial.

ENIGMA Phase 2 Study

Study Design

- Randomized, double-blind, placebo-controlled study in EG/EGE
- Active moderate to severe symptoms
- Biopsy confirmed EG/EGE
  - Stomach: ≥30 eos/high powered field (hpf) in 5 hpfs
  - Duodenum: ≥30 eos/hpf in 3 hpfs
- 65 Patients – 3 arms
  - 22 patients 0.3, 1.0, 1.0, 1.0 mg/kg
  - 21 patients 0.3, 1.0, 3.0, 3.0 mg/kg
  - 22 patients placebo
- 4 monthly doses
- Endpoints assessed two weeks after last dose

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #6: The unexplained, last minute expansion of the ENIGMA trial

However, as of January 4th, 2019, the ClinicalTrials.gov page for the ENIGMA trial still indicated a total of 60 patients. The site indicates that this was the last update to the page until August 5, 2019, the day the study results were publicly released.

Compare v20 to v21

Changes (Side-by-Side) for Study: NCT03496571
January 4, 2019 (v21) -- August 5, 2019 (v22)

No more versions to compare

Changes in: Study Status, Contacts/Locations and Study Design

Show only changed modules

	January 4, 2019	August 5, 2019
Study Identification		
Unique Protocol ID:	AK002-003	AK002-003
Brief Title:	A Study of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis (ENIGMA)	A Study of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis (ENIGMA)
Official Title:	A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacodynamic Effect of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis	A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacodynamic Effect of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis
Secondary IDs:		
Study Design		
Study Type:	Interventional	Interventional
Primary Purpose:	Treatment	Treatment
Study Phase:	Phase 2	Phase 2
Interventional Study Model:	~~Parallel~~ Assignment	Parallel Assignment
Number of Arms:	3	3
Masking:	QuadrupleParticipant, Care Provider, Investigator, Outcomes Assessor	QuadrupleParticipant, Care Provider, Investigator, Outcomes Assessor
Allocation:	Randomized	Randomized
Enrollment:	~~60~~ [~~Anticipated~~]	*65* [*Actual*]

** Emphasis ours*

** Only red box is ours, rest are tracked changes shown on ClinicalTrials.gov*

Source: ClincialTrials.gov page for ALLK ENIGMA P2 trial, showing changes between January 4, 2019 (the last version online prior to the final version modified on August 5, 2019, the day the trial results were publicly released), https://clinicaltrials.gov/ct2/history/NCT03496571?A=21&B=22&C=Side-by-Side#StudyPageTop

Warning sign #6: The unexplained, last minute expansion of the ENIGMA trial

Companies typically disclose trial size expansions, but we can find no such disclosure by Allakos prior to the final trial results, even at its Investor Day on February 19, 2019, where it again stated that the trial was powered with 60 patients. We note that the analyst day occurred deep into the trial and only a few months before it ended.

"Moving on now to the design of the various studies, the eosinophilic gastritis and gastroenteritis study, randomized, double-blind, placebo-controlled, agreed with the FDA, looking at ***a total of 60 patients*** *of 3 arms, 2 active doses…."* – Allakos CMO comments at analyst day

Eosinophilic Gastritis ± Gastroenteritis Phase 2 Study

Design	Key Endpoints		Status
• Randomized, DB, placebo-controlled study • 60 Patients – 3 arms – 20 patients 0.3, 1.0,1.0, 1.0 mg/kg – 20 patients 0.3, 1.0, 3.0, 3.0 mg/kg – 20 patients placebo • Multiple doses (x4) • 9 month safety exposure trial	**Primary**	• Change in eosinophils per high powered field from gastric and/or duodenal biopsies	• Top line data expected Mid 2019
	Secondary	• Change in symptoms from proprietary PRO questionnaire: – Abdominal pain, nausea, diarrhea, vomiting, fullness before finishing a meal, loss of appetite, abdominal cramping, bloating, and diarrhea • Assessment of comorbid EoE	

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019003232/allk-ex991_199.htm ; red ours for emphasis.

Warning sign #6: The unexplained, last minute expansion of the ENIGMA trial

This is problematic as patients enrolled after February/March lacked time to complete the pre-specified protocol by the study's June 24th completion date. The protocol specifies a 28-day screening period, with the primary and secondary endpoints measured at days 99 and 141, respectively, after the screening period ended. This implies 127 days for the primary endpoint (28 + 99, or 18 weeks) and 169 (28 + 141, or 24 weeks) for the secondary. Even if all five patients were magically added on February 20th - implausible given the rarity of EG/EGE and difficulty in finding participants - day 0 wouldn't have begun until March 19th, followed by a 24 week period which by our calculation would have pushed them into September.

ClinicalTrials.gov

Home > Search Results > Study Record Detail Save this study

Trial record 2 of 8 for: allakos

◂ Previous Study | Return to List | Next Study ▸

A Study of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis (ENIGMA)

Tissue eosinophils/hpf to be measured at day 99/week 14

PRO symptoms to be measured at day 141/week 20

Outcome Measures

Primary Outcome Measures :

1. The efficacy of AK002 in patients with Eosinophilic Gastritis (EG) and/or Eosinophilic Gastroenteritis (EGE) as estimated by number of eosinophils per high power field (HPF) in gastric and/or duodenal biopsies before and after receiving AK002 or placebo. [Time Frame: Day 0 (baseline) to Day 99]

Secondary Outcome Measures :

1. Changes in symptoms of EG and/or EGE in a Patient Reported Outcome (PRO) questionnaire [Time Frame: Day -28 (Screening) to Day 141 (End of Study)]

Source: https://clinicaltrials.gov/ct2/show/NCT03496571?term=allakos&draw=2&rank=2; red ours for emphasis.

Warning sign #6: The unexplained, last minute expansion of the ENIGMA trial

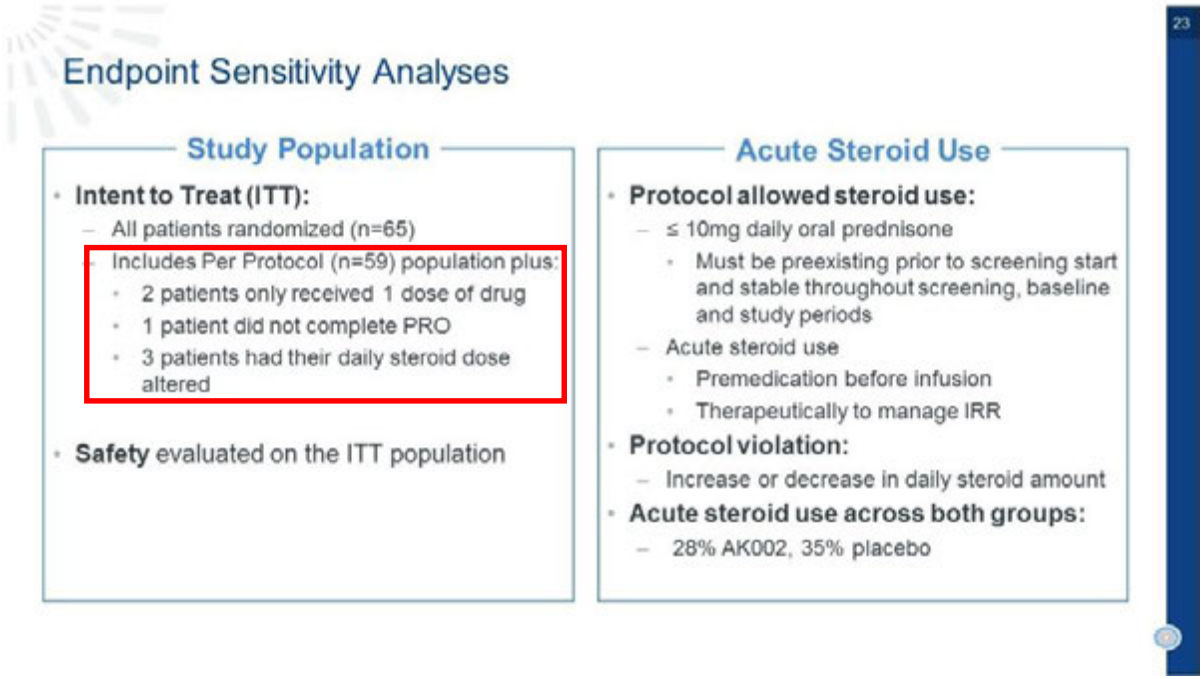
ENIGMA trial investigators we spoke with confirmed the durations of various steps in the study, such as at least a 28 day screening period and six to eight weeks just to get to the first of four monthly infusions, and follow up periods thereafter. The ENIGMA page at the NIH clinical trials website – one of the locations for the study - stated that the protocol required 9 visits over 25 weeks, or >6 months. We fail to see how patients enrolled after late February 2019 would have had time to complete the study's protocol by June 24th.

*"**The patients got paperwork at day minus 28**, have symptoms, and then have to set up for an EGID scope and get biopsies. **Then you have to make sure they qualify on biopsies and qualify for the infusion. It takes at least six to eight weeks to get from start to the first infusion**. They have to do a good diary. **The diary has to be for 28 days before the first infusion**. It takes about four to five months, and then follow up for a couple of weeks to a month. They track them longer." – **Allakos ENIGMA trial investigator***

Source: Seligman expert consultation; NIH ENIMGA trial page (link documented and saved in our notes, but URL appears to no longer resolve): https://clinicalstudies.info.nih.gov/ProtocolDetails.aspx?A_2019-I-0008.html

Warning sign #6: The unexplained, last minute expansion of the ENIGMA trial

After apparently adding 5 patients sometime after February 19, 2019, Allakos then excluded 6 patients. The Intent To Treat (ITT) group was 65, while Per Protocol (PP) was 59. The explanations for why these patients were excluded are amazingly vague. For example, Allakos says that 2 patients were excluded because they "only received 1 dose of drug." Why did they only receive 1 dose – did Allakos, in running the study themselves, see PRO symptoms worsen – or drug-related adverse effects - and kick them out? We note the ITT symptom score p-value failed in the low dose arm and was barely statistically significant in the high dose arm with a p-value of .026, which we believe to be driven by one outlier patient, as we shall detail. The PP symptom score p-value of .0012 looks optically impressive but we question the gymnastics required to get there. We further caution that the bulk of the charts in the ENIGMA top-line results use the PP population of 39 AK002 patients, excluding 4 patients on drug, and exclude 1 patient from the placebo comparisons.



Source: ttps://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #6: The unexplained, last minute expansion of the ENIGMA trial

Mid-trial study adjustments - 11th hour in this case - which expand the sample size and powering are a red flag, as they suggest that the study is failing to show statistical significance. Companies try to salvage the study by enrolling more subjects in the hope that a larger N will capture a smaller effect. We have historically found such modifications to be predictive of trial failure, with shares often declining upon these disclosures. Common sense indicates that if a study is pointing to efficacy, a public company has little incentive to expand the sample size and rock the boat. The sequence here is troubling: Allakos had real-time data as they ran the study themselves; then appear to have quietly expanded the trial size; new patients lacked time to complete the protocol; then some patients were excluded in the PP analysis; and the trial appears to have barely scraped over the finish line with one or two patients driving statistical significance, as we detail in a later section. We share the concerns of a biostatistician, known for identifying fraud in clinical trials, who we engaged to analyze the ENIGMA results.

"A number of studies have been published that show poor study outcomes when patients are being added mid-trial. *This is always criticized and some people take the view that the results can't be trusted.* ***You're getting results, and then changing the protocol and adding more patients. Adding more patients suggests that it was done with knowledge of day to day data."***

"A lot of the results Allakos presents weren't planned beforehand*. They're just showing things that support the drug. There's no detail on the all the methods commonly used to limit bias. It seems reasonable to assume that they had access to patient by patient results.* ***It's just another thing that detracts from showing that the results are a true representation of the drug. They inserted inclusion and exclusion criteria that weren't specified initially. I wonder if they retrospectively applied the inclusion and exclusion criteria."*** ***- Biostatistician and expert in clinical trial fraud***

Source: Seligman expert consultation

Warning sign #7: The ENIGMA trial allowed steroid use in a liberal, widespread manner, rendering the results utterly flawed and compromised as steroids are the standard of care for EG/EGE and rapidly reduce eosinophil levels and symptoms. Biostatisticians, trial design experts, and ENIGMA trial investigators echoed concerns of steroids as a confounding factor. Absurdly, greater than 10mg of Prednisone use was an exclusion criteria, yet doctors pre-dosed patients with an amount 8X or higher prior to infusion of AK002.

Evan Dellon, a principal investigator for the trial, indicated during the Q&A at his October 29, 2019 ACG presentation that the protocol was modified to allow 125mg of Solumedrol prior to infusion. Solumedrol is similar to prednisone but stronger, with a 125mg dose equivalent to 156mg of prednisone. The only 100mg prednisone formulation we could locate online is for horses[1].

Given that steroids are the first line of treatment in EG/EGE and are extremely effective in rapidly and significantly reducing eosinophil levels and in driving symptom improvement, their usage muddies the waters and makes it impossible to determine whether AK002 or steroids drove the purported improvements. Whether this was intentional feature in order to create "positive" results or an accidental flaw and confounding factor is for investors to independently determine.

Allakos has yet to explain the manner in which steroids were used – for example, duration, dosing, etc. The lack of data continues the company's pattern of withholding basic, essential information and prevents investors from assessing the study's results.

Source: [1]https://www.wedgewoodpharmacy.com/items/prednisone-oral-suspension.html; ACG meeting Q&A; Seligman research.

Warning sign #7 (cont'd): The ENIGMA trial allowed steroid use in a liberal, widespread manner, rendering the results utterly flawed and compromised

The company appears keenly aware of the importance of this data, and threw a bone to investors in the August 5th presentation by including P-values for a "no steroids" subgroup. In our opinion, this "data" is merely a cynical attempt to reassure investors, as the more critical subgroup – which was striking by its absence – is the "steroids" subgroup.

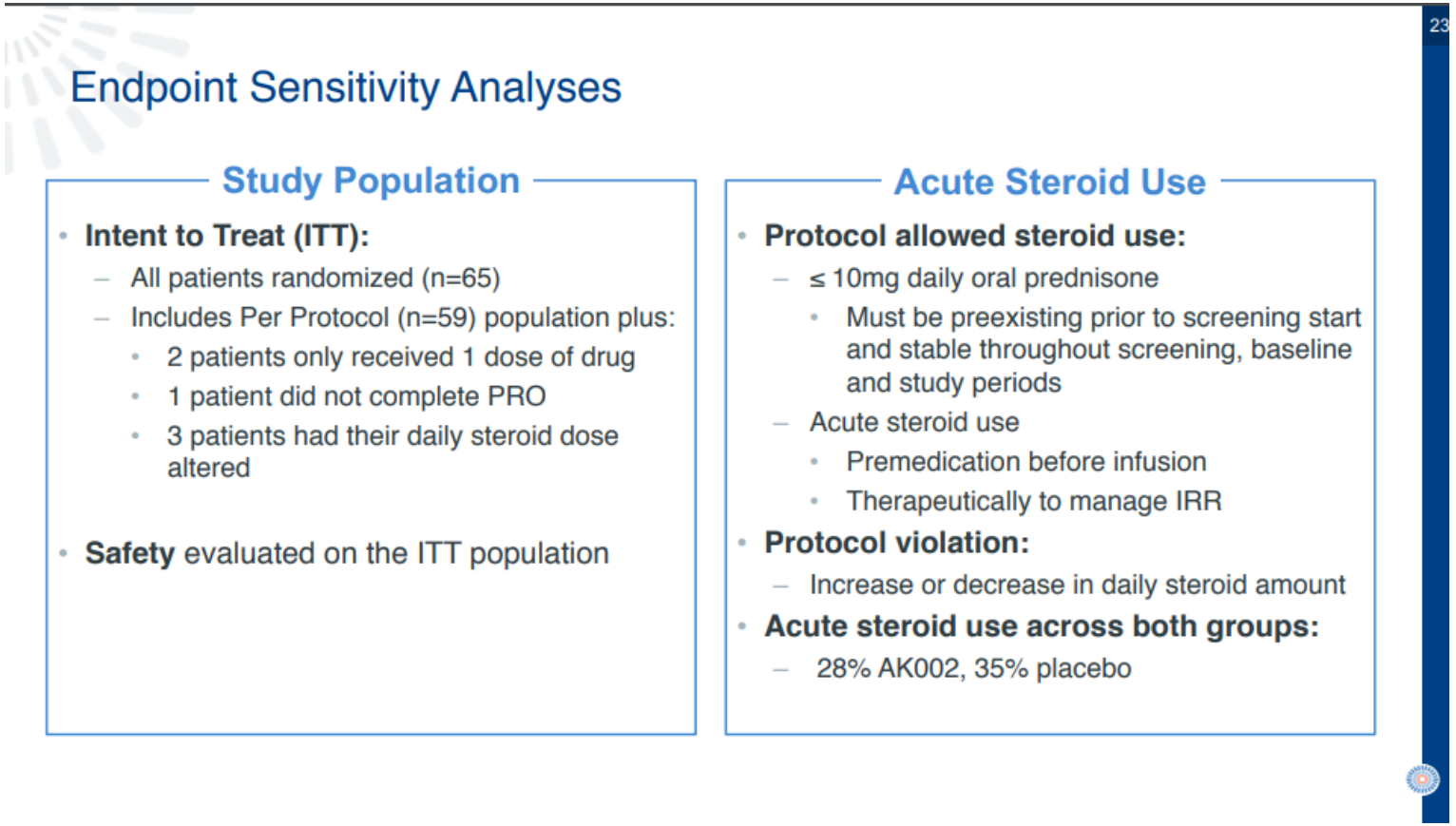
We asked the CEO in August, during a group meeting, whether this data would be shared. He displayed what we would describe as contempt at the notion that steroid use had anything to do with the outcome. He stated that Allakos had shared more data with investors than anyone and that the only reason more steroid data wasn't shared was because investors said they didn't need it, adding that if they wanted the data, he'd share it in September when ALLK visited New York[1]. The company then appeared to be a no-show at a key healthcare conference in NYC a few weeks later.

No such data has been publicly shared as far as we can tell, and two recent medical conference presentations on the EG/EGE study – rather than providing additional data on steroid usage – removed even the superficial steroid-related information in the August 5th top-line presentation. Moreover, the August 5th ENIGMA presentation appears to have been removed from the ALLK site as of the date of this report, and replaced by a much shorter version presented at ACG in late October.

Source: [1]CEO comments from August 2019 broker-sponsored meeting. Comments are paraphrased from notes, not a precise transcript, subject to errors typical of such recollection, and may not be relied upon as an accurate rendition of statements made.

Warning sign #7: Steroid use renders the results flawed and compromised

The EG/EGE study protocol allowed steroid use in at least three different settings: 1) continuation of previous, ongoing usage by the patient; 2) acute administration to medicate patients prior to AK002 infusions; and 3) acute usage to manage side effects from the infusion. Given the widespread use of steroids and their prominence as a confounding factor, the ambiguity of the disclosures below is remarkable: what dosages were used prior to infusion? Were steroids given prior to every infusion, and to every patient? What dosages were given to manage reactions? What was the duration of usage?



Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm

Warning sign #7: Steroid use renders the results flawed and compromised

Allakos attempted to preempt the inevitable questions on steroids by including P-values for a "No Steroids" subgroup. However, it is unclear how "no steroids" is defined and whether these patients were allowed to use or were administered steroids in some settings but not others. If so, this would render the slide even more irrelevant and evasive.

What does "no steroids" mean? No definition is provided.

All Analyses Show Consistent Results

Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	AK002 Dose Groups Low (n=19/12/22)	AK002 Dose Groups High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	ITT	0.0260	0.1556	0.0359	-

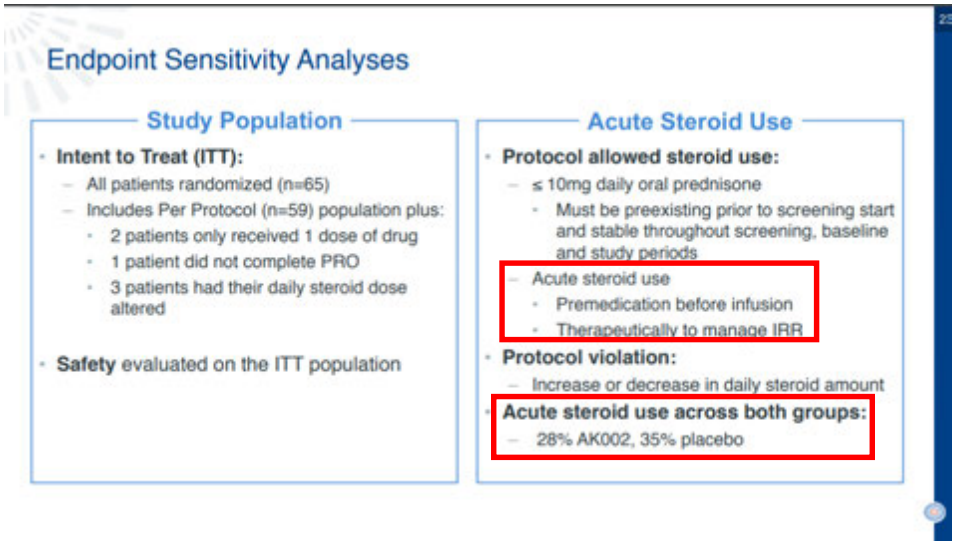
24

Allakos

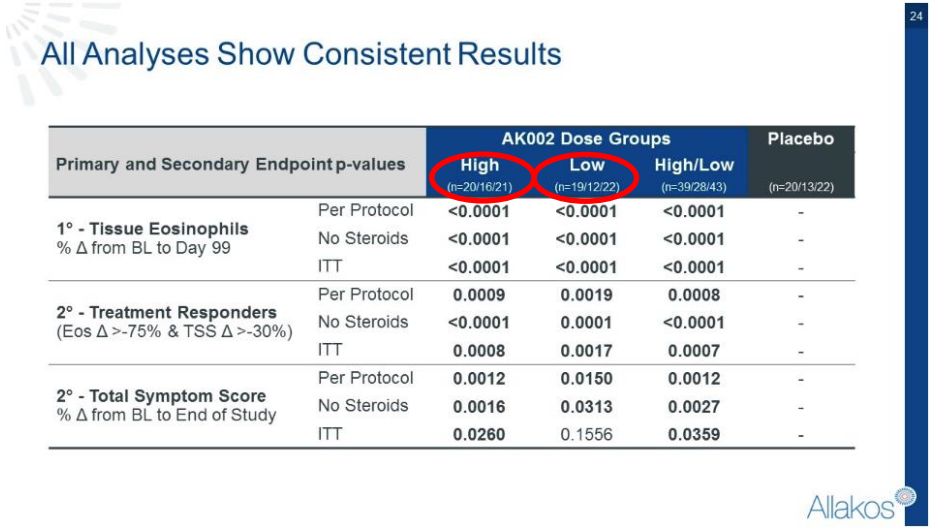
Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #7: Steroid use renders the results flawed and compromised

We are concerned that Allakos' steroid figures don't reconcile with common sense. One slide states 28% "acute steroid use" across the AK002 arms, or 12 patients overall using n=43. Acute appears to be defined as prior to infusion or to manage infusion-related reactions. However, the next slide implies that there were 15 patients in total (10 low dose, 5 high dose) with any steroid use in active arms. In other words, Allakos appears to be representing that only 3 patients out of 43 total in the active arm received non-acute (i.e., chronic) steroid therapy. This figure strikes us as wildly inaccurate and implausible. Allakos' own trial investigators indicated to us that 80% of patients are typically on steroid therapy, and Allakos' figure is inconsistent with Facebook posts from numerous patients in their trial. As a result, we believe that Allakos is under-representing the usage and impact of steroids.



- 28% "acute steroid use" in AK002 arms



Primary and Secondary Endpoint	p-values	AK002 Dose Groups: High (n=20/16/21)	AK002 Dose Groups: Low (n=19/12/22)	AK002 Dose Groups: High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	ITT	0.0260	0.1556	0.0359	-

- High dose arm: ITT (n=21) less no steroids (n=16) implies n=5 steroid patients
- Low dose arm: ITT (n=22) less no steroids (n=12) implies n=10 steroid patients

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #7: Steroid use renders the results flawed and compromised

Irrespective, displaying P-values for a "no steroids" subgroup fails to answer the critical question. The subgroup which matters is the "steroids" subgroup. In other words, was AK002 statistically significant in reducing eosinophils and symptoms in patients who are taking steroids, relative to placebo? These patients represent the vast majority of the EGID real-world population. We believe it is no accident that Allakos withheld p-values for the "steroids" cohort in each arm. The omission of efficacy data for placebo patients on steroids is striking – because, we believe, the data would show no relative benefit from AK002.

Where is the missing row for the "Steroids" subgroup, especially for placebo patients?

All Analyses Show Consistent Results

Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	AK002 Dose Groups Low (n=19/12/22)	AK002 Dose Groups High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	Steroids	----???-----	----???-----	----???-----	----???-----
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	Steroids	----???-----	----???-----	----???-----	----???-----
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	Steroids	----???-----	----???-----	----???-----	----???-----
	ITT	0.0260	0.1556	0.0359	-

24

Allakos

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #7: Steroid use renders the results flawed and compromised

The small fragment of steroids data which Allakos did present is worrisome and makes no sense. It suggest that steroids made symptoms worse, which is absurd as steroids are the standard of care and drive symptom improvement in the vast majority of patients. Note the large decline in efficacy between the low dose ITT and "no steroids" groups in total symptom score, from .0313 to .1556. In other words, patients without steroids supposedly improved, but when 10 patients with steroids are added back (i.e., the ITT group), the p-value drops to .1556 and is no longer statistically significant.

All Analyses Show Consistent Results

Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	AK002 Dose Groups Low (n=19/12/22)	AK002 Dose Groups High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	**<0.0001**	**<0.0001**	**<0.0001**	-
	No Steroids	**<0.0001**	**<0.0001**	**<0.0001**	-
	ITT	**<0.0001**	**<0.0001**	**<0.0001**	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	**0.0009**	**0.0019**	**0.0008**	-
	No Steroids	**<0.0001**	**0.0001**	**<0.0001**	-
	ITT	**0.0008**	**0.0017**	**0.0007**	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	**0.0012**	**0.0150**	**0.0012**	-
	No Steroids	**0.0016**	**0.0313**	**0.0027**	-
	ITT	**0.0260**	0.1556	**0.0359**	-

Allakos

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #7: Steroid use renders the results flawed and compromised

A similar absurdity is visible in the high dose cohort, which also shows a sharp drop in efficacy when patients on steroids are added back. The no steroids p-value is .0016, but falls to .026 when 5 patients are included to get to ITT. Furthermore, the high dose arm had few patients on steroids (n=5) compared to the low dose arm (n=10). The low dose arm - with double the number of steroid patients - failed to show statistically significant symptom improvement, again indicating that steroids led to a worsening of symptoms, which is odd and counter to clinical understanding and experience. It suggests that patients must discontinue steroids for AK002 to work, an absurd notion as they're the standard of care and prescribed to 80% of patients - according to Allakos' trial investigators that we consulted.

All Analyses Show Consistent Results

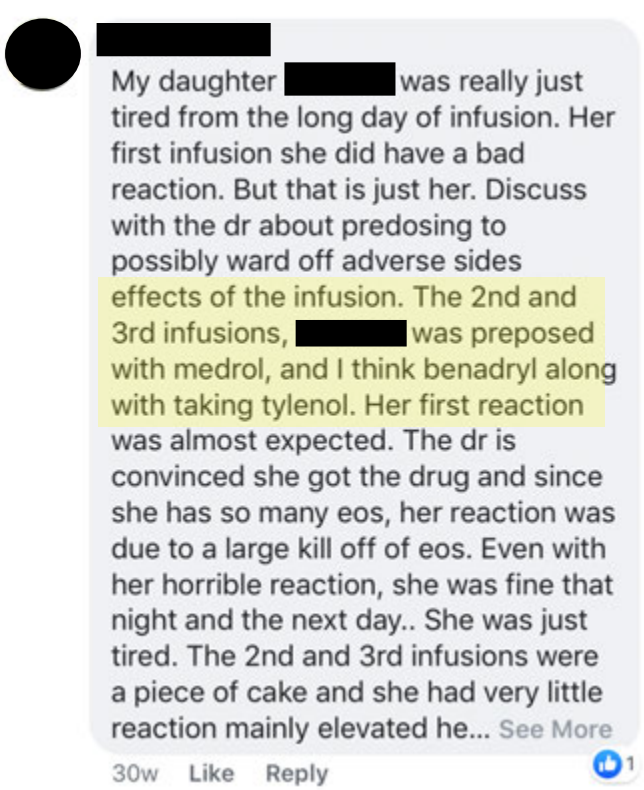
Primary and Secondary Endpoint p-values		AK002 Dose Groups			Placebo
		High (n=20/16/21)	Low (n=19/12/22)	High/Low (n=39/28/43)	(n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	**<0.0001**	**<0.0001**	**<0.0001**	-
	No Steroids	**<0.0001**	**<0.0001**	**<0.0001**	-
	ITT	**<0.0001**	**<0.0001**	**<0.0001**	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	**0.0009**	**0.0019**	**0.0008**	-
	No Steroids	**<0.0001**	**0.0001**	**<0.0001**	-
	ITT	**0.0008**	**0.0017**	**0.0007**	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	**0.0012**	**0.0150**	**0.0012**	-
	No Steroids	**0.0016**	**0.0313**	**0.0027**	-
	ITT	**0.0260**	0.1556	**0.0359**	-

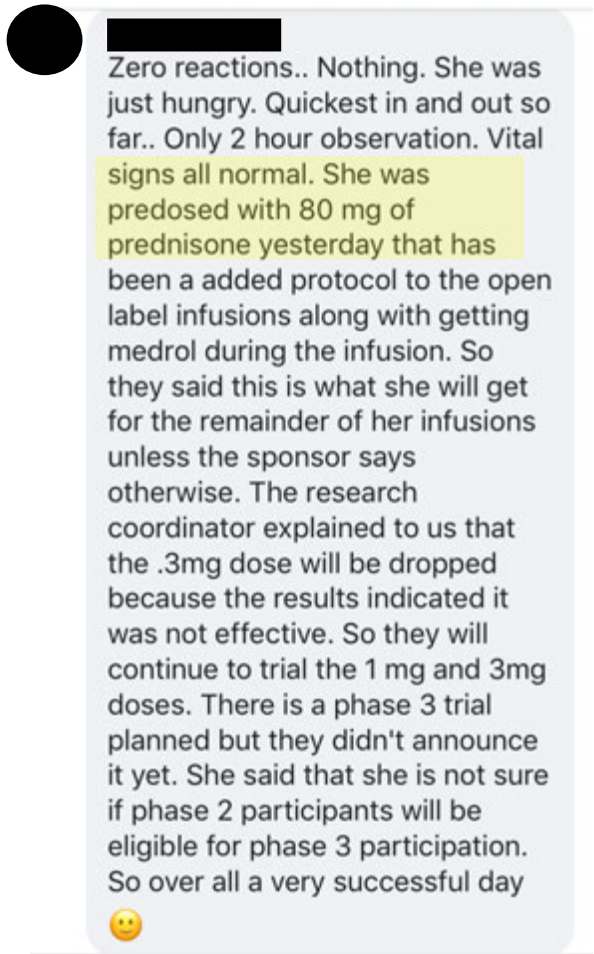
Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; Seligman expert consultations; red ours for emphasis.

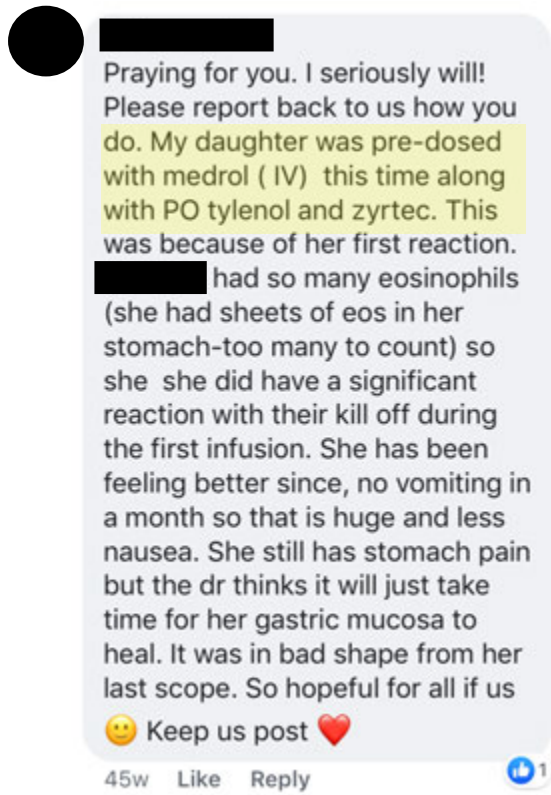
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #7: Steroid use renders the results flawed and compromised

Our research suggests that steroid use was a defining feature of the trial. Participants were prolific in posting their real-time experiences on a Facebook group for eosinophilic gastritis. The posts indicate pre-dosing prior to AK002 infusions with steroids such as prednisone, Medrol (25% more potent than prednisone), as well as antihistamines such as Benadryl and Zyrtec, not to mention Tylenol and perhaps other undisclosed medications that can sway patient-reported symptom scores. The open label extension study appears to be now pre-dosing patients with a whopping 80 mg of prednisone – 8X the daily 10 mg dose listed as an exclusion criteria in the ENIGMA protocol.





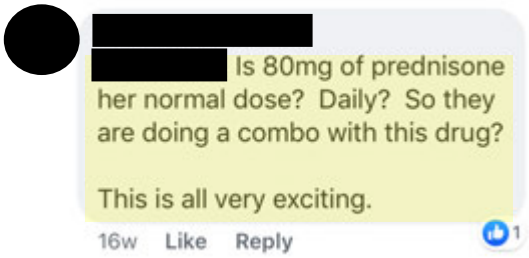


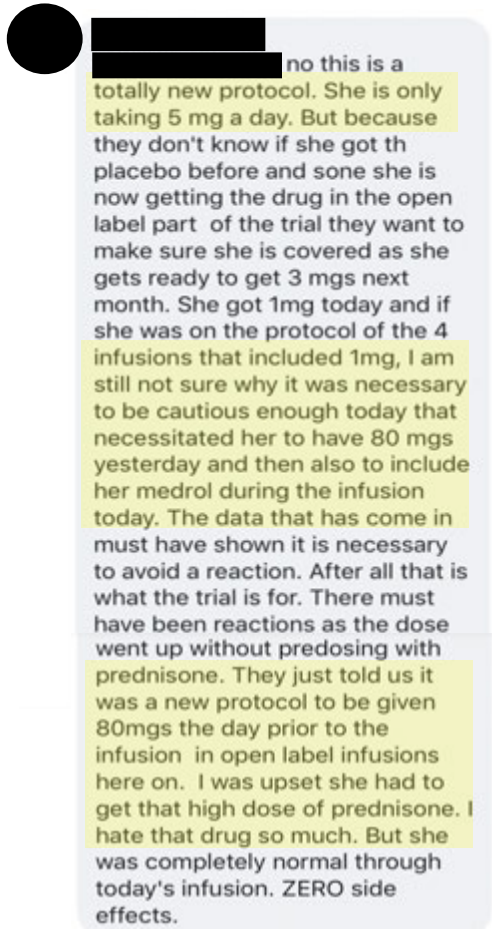
Source: https://www.facebook.com/groups/258285487951166/

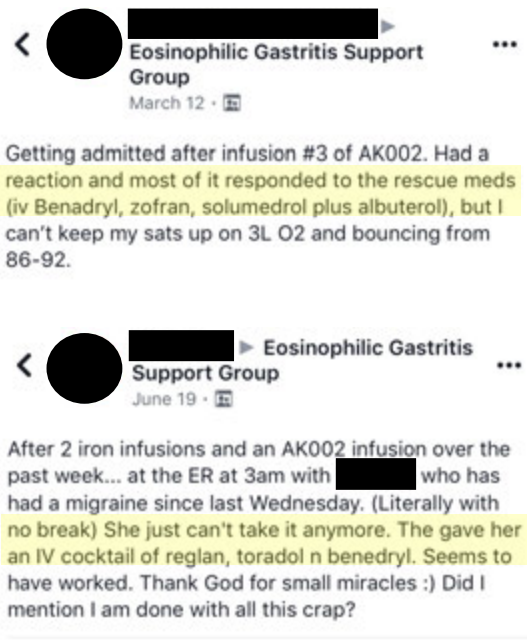
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #7: Steroid use renders the results flawed and compromised

The doses of prednisone are so high that patients are wondering if steroids are a combo therapy for the trial. Others are "upset" at 'that high dose of prednisone" and note the daily usage of steroids in addition to pre-dosing prior to infusions. Group members also posted about medications given after infusion reactions: Medrol, albuterol, Benadryl, Zofran, Toradol, and Reglan. With steroids as ongoing medication, heavy steroid doses pre-AK002, and then infusions of various drug cocktails after infusion reactions, we wonder how Allakos can claim that AK002 drove purported symptom score improvements vs. these drugs.







Source: https://www.facebook.com/groups/258285487951166/

Warning sign #7: Steroid use renders the results flawed and compromised

We spoke to investigators in the AK002 study who confirmed the color from patients on Facebook and indicated that steroid usage was essentially as their discretion as physicians. The doses appear to be all over the place, further illustrating the sloppy and compromised nature of the trial. One made a comment highlighting the magnitude of the dosage.

"We did 20 mg of prednisone before the infusion. ***You could give it clinically as the doctor if you wanted to. Everyone got it.*** *For the first infusion and maybe after the first. If the patient had a reaction, could give prednisone then also.* ***The protocol was the first two infusions but you could give it for the third or fourth infusions."*** *– ENIGMA trial investigator*

"I had a choice to put patients on steroids or not. Some I did and some I didn't. We used 80mg of prednisone. If you give 40mg of prednisone and then stop it suddenly it risks kidney problems." *– ENIGMA trial investigator*

Source: Seligman expert consultations

Warning sign #7: Steroid use renders the results flawed and compromised

Widespread, uncontrolled steroid use poses a massive flaw in the Allakos trial, as they are the standard of care for EG/EGE patients and are effective in 90% of patients. Even small doses – 5mg/day, well below the 10mg dosage allowed for chronic usage in the AK002 trial, not to mention a fraction of the 80mg used prior to infusion – can induce rapid, sustainable reductions in eosinophils and clinical symptoms, within 2-14 days.

An NIH paper indicates that doses of prednisone well below those used in the AK002 trial are sufficient to induce *"dramatic clinical improvement in 2-14 days."*

"Newly diagnosed [EG/EGE] patients are almost always responsive to systemic corticosteroid therapy […] Doses of prednisone of 0.5–1 mg/kg typically induce a dramatic clinical improvement in 2–14 days. As such, short-term treatment with systemic corticosteroids is an excellent means to induce clinical remission."

Source: *"Eosinophilic Gastroenteritis and Related Eosinophilic Disorders,"* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130565/pdf/nihms587639.pdf

Another paper indicated that 90% of patients respond to steroid therapy and that even a 5 mg/day maintenance dose suppressed symptoms. Note the paper abbreviates prednisone as "PSL."

diets are often poor [6]. The next step is the use of steroids, which have been a mainstay of treatment in EGE. The dosage of PSL given at the onset of the condition is 20 to 40 mg/day for 6 to 8 weeks [6]. About 90% of patients respond to this therapy [7]. If patients require high

The clinical course of the disease is shown in Fig. 4. The patient was treated with prednisolone (PSL) at 40 mg/day for 2 weeks which led to a rapid improvement in the symptoms and the eosinophil counts (0/mm^3). PSL was then tapered to 20 mg/day and the patient was discharged from hospital. After discharge, the PSL dose continued to be tapered uneventfully until the dose reached 3 mg/day, at which point the abdominal pain recurred and there was a rapid increase in the peripheral eosinophil counts (9,772/mm^3; first relapse). The PSL dose was therefore increased to 20 mg/day, which caused a rapid improvement of eosinophilic counts (99/mm^3). However, when PSL was tapered again to a maintenance dose of 5 mg/day, eosinophil counts began to increase without symptoms (second relapse). Because

Source: *"Successful Treatment of Eosinophilic Gastroenteritis with Clarithromycin*," https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3529245/; red ours for emphasis.

Warning sign #7: Steroid use renders the results flawed and compromised

In addition to eosinophilic gastritis and gastroenteritis, steroids are extremely effective in eosinophilic esophagitis. Studies on steroid potency for EGID's are easy to locate. As an example, we note a pediatric study evaluating prednisone versus topical steroids in EGE which indicated that 100% of patients in the prednisone arm were symptom-free within four weeks. Biopsies measuring eosinophils were equally dramatic, with 81% of patients achieving 100% histologic resolution and 94% showing near-total resolution.

Comparison of Oral Prednisone and Topical Fluticasone in the Treatment of Eosinophilic Esophagitis: A Randomized Trial in Children

Background & Aims: Although eosinophilic esophagitis is recognized increasingly, outcome data guiding therapy are limited. We conducted a prospective randomized trial comparing oral prednisone (P) and swallowed fluticasone (F) for histologic and clinical response. ***Methods:*** Patients were randomized to receive P or F for 4 weeks, followed by an 8-week weaning protocol. Esophageal histology was evaluated at baseline and after 4 weeks of therapy. Clinical assessments were performed at weeks 0, 4, 12, 18, and 24. ***Results:*** Eighty patients with eosinophilic esophagitis were enrolled: 40 in the P arm and 40 in the F arm. Histologic improvement was seen in 30 of 32 P and 34 of 36 F patients, with a greater degree of histologic improvement in the P group. All P and 35 of 36 F patients were free of presenting symptom(s) at week 4. Symptom relapse was seen in 45% of patients by week 24. Kaplan–Meier analysis showed no difference between P and F with regard to relapse rate ($P = .7399$). No significant difference in time to relapse was found between groups ($P = .2529$). Systemic adverse effects were noted in 40% of the P arm, whereas esophageal candidal overgrowth was seen in 15% of the F arm. ***Conclusions:*** Systemic and topical corticosteroids were effective in achieving initial histologic and clinical improvement. P resulted in a greater degree of histologic improvement, without evidence of an associated clinical advantage over F in terms of symptom resolution, relapse rates, or time to relapse. Symptom relapse was common to both groups upon therapy discontinuation, highlighting the need for maintenance treatment protocols.

Results: Eighty patients with eosinophilic esophagitis were enrolled: 40 in the P arm and 40 in the F arm. Histologic improvement was seen in 30 of 32 P and 34 of 36 F patients, with a greater degree of histologic improvement in the P group. All P and 35 of 36 F patients were free of presenting symptom(s) at week 4. Symptom relapse was

Source: https://www.cghjournal.org/article/S1542-3565(07)01104-4/pdf; red ours for emphasis.

Warning sign #7: Steroid use renders the results flawed and compromised

We believe Allakos is clearly aware of the problematic nature of steroid use in their EG/EGE trial, as evidenced by data omissions and the withholding of basic information on steroid usage during the trial (dosages, durations, etc.). The company appears to have been so concerned about the confounding effect of steroids that earlier trials excluded their use more broadly. We wonder why the company changed the EG/EGE protocol to allow their use. We note that earlier trials also excluded antihistamine usage, yet they were used during the EG/EGE study.

AK002 Phase 1 safety/tolerability study excluded steroid patients

Exclusion Criteria:

9. Use of immunosuppressants, oral corticosteroids, angiotensin converting enzyme (ACE) inhibitors or beta blockers within 2 weeks or 5 half-lives (whichever is longer), prior to Screening.

Source https://clinicaltrials.gov/ct2/show/NCT02859701?term=allakos&draw=2&rank=6

Failed AK001 Phase 2 study in nasal polypsis excluded steroid patients

Exclusion Criteria:

- Use of systemic corticosteroids within 6 weeks of screening

Source: https://clinicaltrials.gov/ct2/show/NCT02734849?term=allakos&rank=8

AK002 Phase 1 in ISM excluded patients requiring more than 10mg of steroids, yet the EG/EGE trial allowed far higher doses in multiple contexts.

Exclusion Criteria:

9. Use during the 30 days before Screening (or 5 half lives, whichever is longer) or expected to require the use of omalizumab, immunosuppressive drugs, or systemic corticosteroids with a daily dose >10 mg prednisone or equivalent

Source: https://clinicaltrials.gov/ct2/show/NCT02808793?term=allakos&draw=2&rank=7

**All red ours for emphasis*

Warning sign #7: Steroid use renders the results flawed and compromised

We note the muddying effect of antihistamines and other medications administered, beyond just steroids. The EG/EGE trial protocol specifically prohibited the use of other medications that may interfere with the study, but only during the screening period and appears to allow their usage thereafter during the trial. We find this disturbing, as it lowers the bar while establishing baseline scores, while allowing medications in combination with AK002 as symptom improvements were measured.

ENIGMA EG/EGE trial page on ClinicalTrials.gov

Exclusion Criteria:

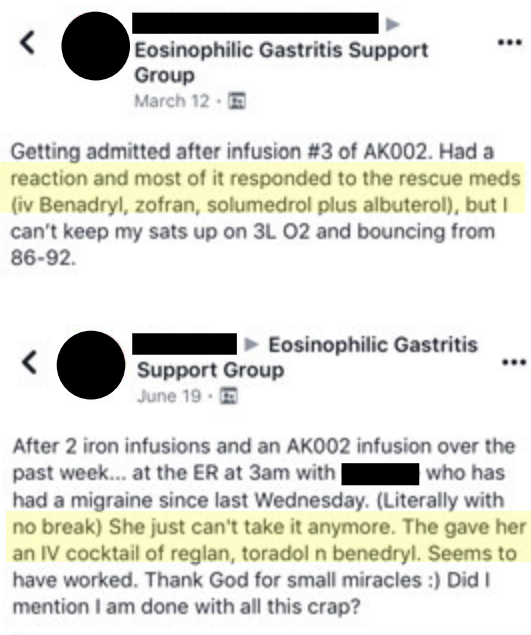
9. Use of any medications that may interfere with the study such as immunosuppressive or immunomodulatory drugs (including azathioprine, 6-mercaptopurine, methotrexate, cyclosporine, tacrolimus, anti-TNF, anti-IL-5, anti-IL-5 receptor, dupilumab, anti-IgE antibodies, omalizumab) or systemic corticosteroids with a daily dose >10 mg of prednisone or equivalent, during 5 half-lives prior to screening or during the screening period, except for omalizumab taken in asthma and/or urticaria patients where their asthma and/or urticaria cannot be controlled on other medications. In such cases, the dose of omalizumab should remain stable during screening and throughout the study.

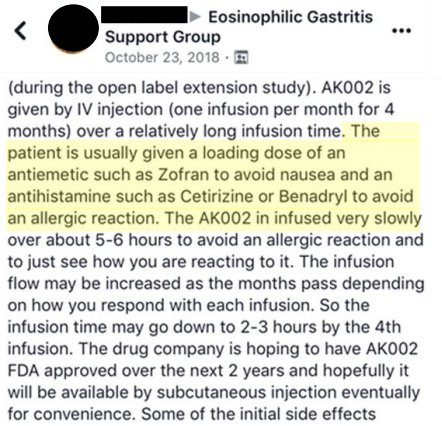
Source: https://clinicaltrials.gov/ct2/show/NCT03496571?term=allakos&draw=1&rank=2; red ours for emphasis.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #7: Steroid use renders the results flawed and compromised

Patients' Facebook posts reveal the administration of non-steroidal drugs such as antihistamines prior to infusion and in other settings during the trial. Numerous studies describe antihistamines' role in managing eosinophilic and mast cell conditions. Posts also mention drugs to treat nausea, vomiting, and gastric emptying – such as Zofran, which one patient began to take daily after vomiting during the trial. Critically, these are three of the eight symptoms measured on the EG/EGE symptom scale. These symptoms would naturally correlate with the remaining ones evaluated, namely abdominal pain, cramping, bloating, and diarrhea. Given the variety of drugs that appear to have been administered liberally during the trial, we struggle to understand how the EG/EGE study singles out the effect of AK002.





Source: https://www.facebook.com/groups/258285487951166/

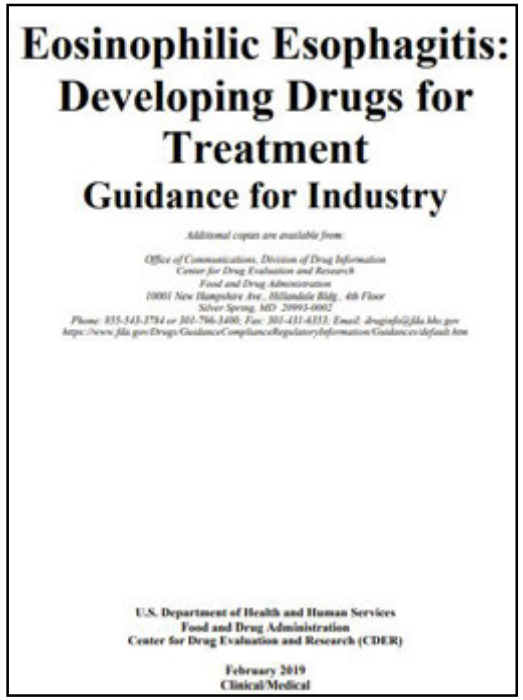
"Eosinophilic Gastroenteritis; Diagnosis and Clinical Perspectives"

"Many therapeutic options are available for the management of EGE *[…] For patients with moderate–severe disease, corticosteroids represent the mainstay of therapy. Since prolonged corticosteroid treatment carries the risk of serious adverse effects, other options with better safety profiles have been proposed. These include budesonide and steroid-sparing agents, such as LT inhibitors, immunomodulators,* ***antihistamines****, and mast-cell stabilizers."*

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6556468/

Warning sign #7: Steroid use renders the results flawed and compromised

We believe the FDA is highly sensitive to the need for steroid controls during EGID studies, presenting obvious problems for Allakos when they engage with the FDA on phase 3 design and endpoints. The reckless approach to steroids used in the phase 2 is almost certainly a non-starter, and without the assist from steroids, we see a disastrous scenario for investors once Allakos attempts to replicate its phase 2 with a real trial. The FDA published a guidance document in February 2019 on eosinophilic esophagitis, which specifically mentions steroid controls. KOL's we have spoken with believe that the FDA has no plans for a separate guidance document on EG and that this EOE document will serve as the template. An FDA speaker – the contact individual listed on the EOE guidance document - reinforced the agency's concerns about steroid use during EGID trials just weeks ago during a presentation at an EGID conference on November 8, 2019.



Eosinophilic Esophagitis: Developing Drugs for Treatment

Guidance for Industry

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353; Email: druginfo@fda.hhs.gov
https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

February 2019
Clinical/Medical

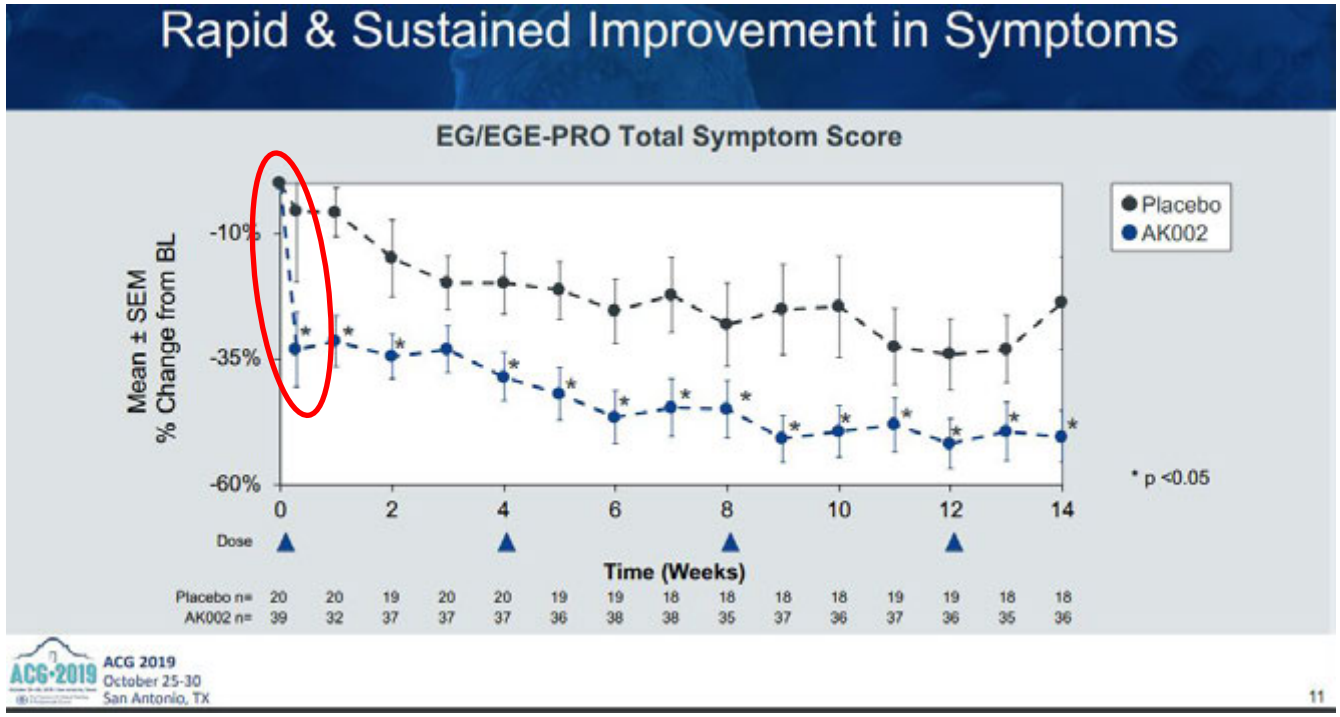
111 • Patients should maintain stable doses of PPI therapies (other than a failed trial of PPI
112 monotherapy at an adequate dose); leukotriene inhibitors; or nasal, inhaled, and/or orally
113 administered locally or topically acting corticosteroid drugs for any condition (such as
114 asthma or allergic rhinitis) preceding enrollment and throughout the duration of the trial
115 period. The trial protocol should specify the statistical plan to account for patients who
116 initiate treatment with systemic corticosteroid drugs during the trial period, as well as
117 those patients who need rescue treatment with topical or locally acting corticosteroid
118 drugs.

Source: FDA EOE guidance document https://www.fda.gov/media/120089/download ; 'FDA Guidance on Eosinophilic Esophagitis," talk on Nov 8, 2019 at 5th Cured EGID Conference, https://www.regonline.com/custImages/460000/465951/2019CUREDAgendawithSpaces.pdf

Warning sign #7: Steroid use renders the results flawed and compromised

One of Allakos own trial investigators stated that steroids could have driven the effects attributed to AK002. Given that steroids can provide an acute benefit within two days per the clinical literature on eosinophilic conditions, we encourage investors to examine the chart below recently posted by Allakos. Note that the majority of the purported symptom improvement occurs within days – within the timeframe for steroid response - after which the placebo and AK002 curves closely track. We struggle to believe how Allakos can claim such rapid resolution after years or decades of chronic damage, but even with the benefit of the doubt Allakos must answer questions raised by their own investigator.

"Could steroids be a confounding factor here? Of course. With 80mg of prednisone, one shot can give you an acute effect." *– Allakos EG/EGE trial investigator*



Source: Seligman expert consultations; http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; red ours for emphasis

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #7: Steroid use renders the results flawed and compromised

Allakos is continuing its EG/EGE study in an open label extension format. We are dumbfounded that the protocol has been changed to remove any exclusion criteria related to steroids or other medications which could muddy the results. Allakos' trial protocols have evolved from allowing no steroid use, to allowing some steroid use, and to now allowing unbridled steroid use. The company appears to have thrown caution and scientific method to the wind, and in our opinion seems fixated on showing AK002 "efficacy" in any way that it can.

ClinicalTrials.gov trial record

Study Design Go to

Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	60 participants
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase 2, Multicenter, Open-Label, Extension Study to Evaluate the Safety and Tolerability of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis
Actual Study Start Date:	November 14, 2018
Estimated Primary Completion Date:	April 2020
Estimated Study Completion Date:	April 2020

Exclusion Criteria:

1. Poor tolerance to previous administration of AK002 in the opinion of the Investigator.
2. Known hypersensitivity to any constituent of the study drug.
3. Any disease, condition (medical or surgical), or cardiac abnormality, which, in the opinion of the Investigator, would place the patient at increased risk.
4. Planned or expected vaccination with live attenuated vaccines during the treatment, or vaccination expected within 5 half-lives (4 months) of AK002 administration.
5. Women who are pregnant, breastfeeding, or planning to become pregnant while participating in the study.
6. Any other reason that, in the opinion of the Investigator or Medical Monitor, makes the patient unsuitable for enrollment.

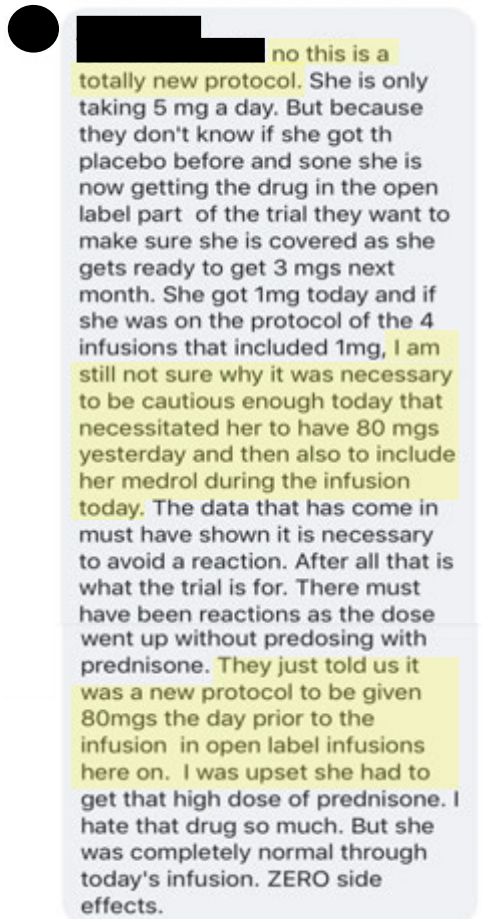
No mention of steroid use as an exclusion criteria.

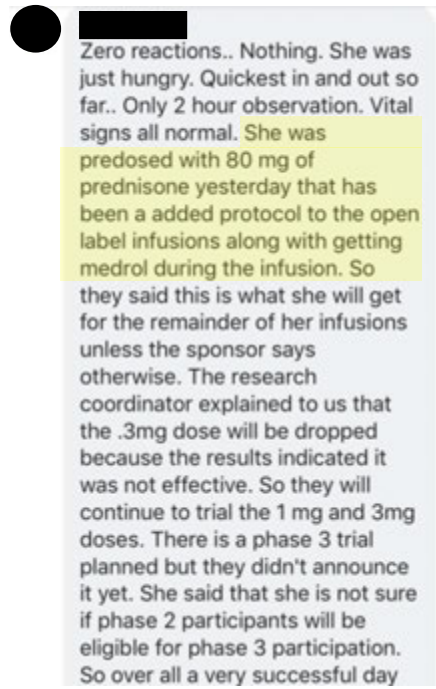
Source: https://clinicaltrials.gov/ct2/show/NCT03664960?term=allakos&draw=1&rank=1; red ours for emphasis.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #7: Steroid use renders the results flawed and compromised

Facebook posts confirm that the open label extension protocol has changed to allow 80mg of prednisone and to also add Solumedrol – a steroid that is 25% stronger than prednisone at equivalent dosage. Steroid doses may be far higher than 80mg, given comments by Evan Dellon, a Principal Investigator of the ENIGMA trial, during the Q&A portion of his presentation at ACG in October, where he indicated that the protocol was modified to allow 125mg of Solumedrol, equivalent to a 156mg dose of prednisone.





Source: https://www.facebook.com/groups/258285487951166/

Warning sign #7: Steroid use renders the results flawed and compromised

We consulted a PhD with expertise in biostatistics and trial design, who conducted acquisition due diligence at one of the largest biotech companies. The expert expressed deep skepticism of the ENIGMA presentation, particularly on the use of steroids. A professor of biostatistics with 20 years of experience, known for identifying discrepancies in clinical trials, echoed similar concerns, as did other scientists, biostatisticians, and experts we spoke with.

"Can we see in the data or can we infer that the results are not due to steroids? The numbers shown here don't answer this question. Showing only p-values on this slide doesn't tell you this." ***- Professor of biostatistics***

"The other thing that really bothers me is the effect of steroids *and how it wasn't standardized between the placebo and active arms. The rationale in providing steroids is to prevent an infusion reaction, but they're giving someone 80 mgs of steroids on top of a normal maintenance dose.* ***The trial protocol says that taking 10mg of prednisone is enough to exclude patients, yet they're giving 80 mg to preventing infusion reaction****, which is only people who need it, which is of course the active arm.* ***This is so confounding that's it's impossible to tell what's causing the benefit. Dosing everyone the day before and then waiting 24 hours is a great way to get symptom reduction. There is just no basis for comparison here.*** *Studies in pediatric patients show steroids lower eosinophils by 90-95%. So what's the effects of Siglec-8 vs. steroids?"* ***– Research scientist***

"P-values are not informative *and no clinician cares. They want to know response rates****. The effect sizes are what matters and they don't show them. Steroids can obscure the results."*** ***- Biostatistician***

"The p-values on page 24 suggest that the delta is a lot smaller if you're already on steroids. It's hard to see a change. The big question is, is this better than steroids? ***They don't show you placebo values because they know that those values show something that they don't want you to see. I've never seen a table of p-values like this.*** *Companies show means and standard deviations and show p-values with an asterisk.* ***This is an odd way to show data****. And to not show placebo values is strange****. It looks to me like they manipulated these numbers to look good. Why didn't they show the data the way it's usually done?"*** ***– PhD/scientist who conducted due diligence at one of the largest biotech companies***

Source: Seligman expert consultations

Warning sign #8: The August 5th ENIGMA topline results provide a master class in fatal discrepancies and internal contradictions. The red flags are so numerous that we consider the presentation to be little more than sleight of hand. We have never seen the sheer number of warning signs in a single trial's results as we do here.

1. The low dose AK002 cohort failed to show statistically significant symptom reduction despite eliminating eosinophils, bewildering trial investigators and undermining the entire Siglec-8 premise upon which Allakos is based.

2. Allakos states that eosinophils actually increased by 10% in the placebo group, yet the placebo group symptoms still improved by 25%, further undermining their entire hypothesis.

3. As another worrisome discrepancy, ENIGMA's table of p-values suggests that steroids made symptoms worse, which is absurd as steroids are the standard of care and drive symptom improvement in the vast majority of patients

4. Despite n=43 in the active arms, one or at most two outlier patients swung the TSS p-values into statistical significance, according to a number of biostatisticians and experts in clinical trial design we asked to analyze the data. Their analyses were unanimous in indicating that the ENIGMA trial barely scraped over the finish line.

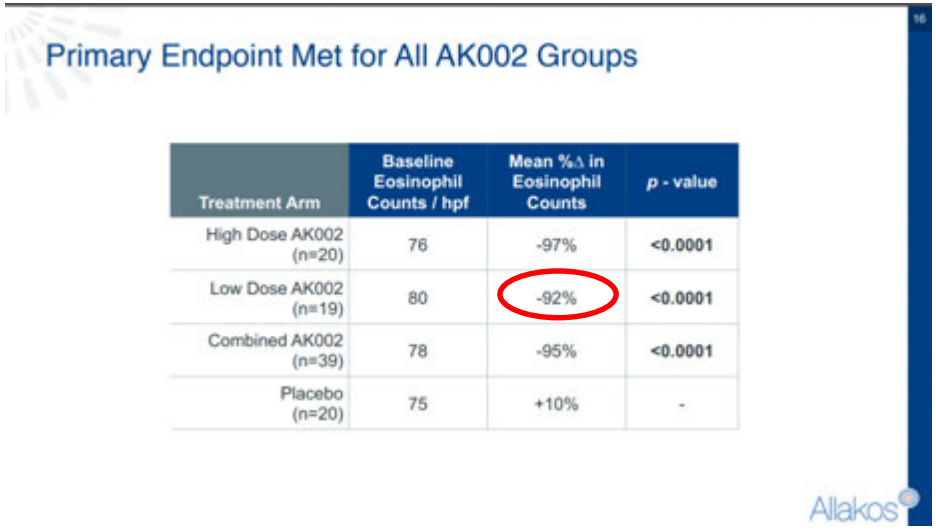
5. Allakos claims that AK002 reduced dysphagia (trouble swallowing) in the EoE subgroup in the EG/EGE trial, yet dysphagia wasn't even a symptom measured in the PRO.

Warning sign #8: Fatal discrepancies and internal contradictions in the ENIGMA data

We have never seen the sheer number of discrepancies and statistical red flags in a single trial's top line results as we do in the ENIGMA read-out. Allakos claims that AK002 reduced tissue eosinophils by 92% in the low dose cohort, close to the high dose cohort reduction of 97%. However, the low dose cohort failed to show statistically significant symptom reduction. If eosinophils are what cause symptoms – the entire theory behind Allakos - why did eliminating eosinophils not show a symptom benefit over placebo? We asked multiple ENIGMA trial investigators to comment and all were bewildered by the paradox. We believe this discrepancy alone undermines the company's Siglec-8 premise.

Allakos claims that low dose of AK002 showed 92% reduction in tissue eosinophils

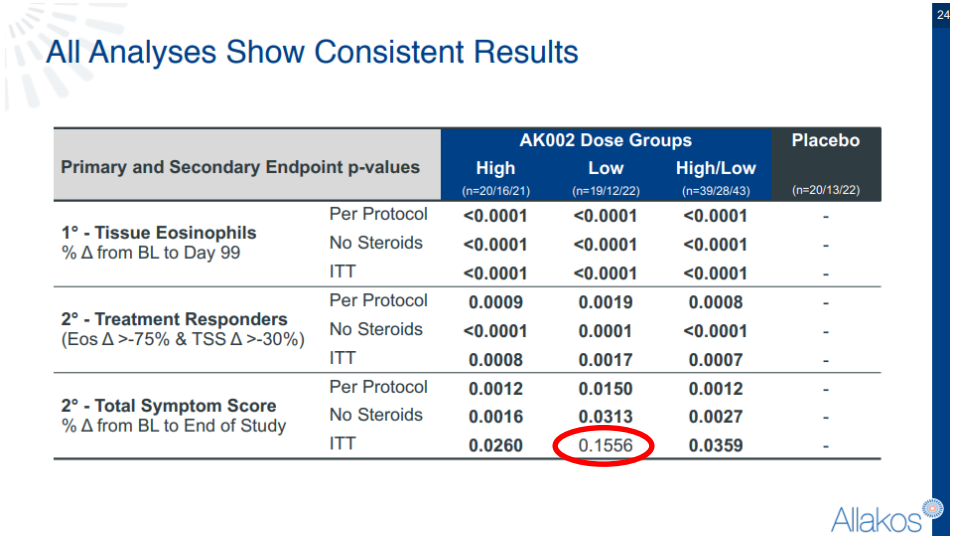
Yet, low dose arm failed flopped on symptom improvement with P-value of .1556



Primary Endpoint Met for All AK002 Groups

Treatment Arm	Baseline Eosinophil Counts / hpf	Mean %Δ in Eosinophil Counts	*p* - value
High Dose AK002 (n=20)	76	-97%	<0.0001
Low Dose AK002 (n=19)	80	-92%	<0.0001
Combined AK002 (n=39)	78	-95%	<0.0001
Placebo (n=20)	75	+10%	-

Allakos



All Analyses Show Consistent Results

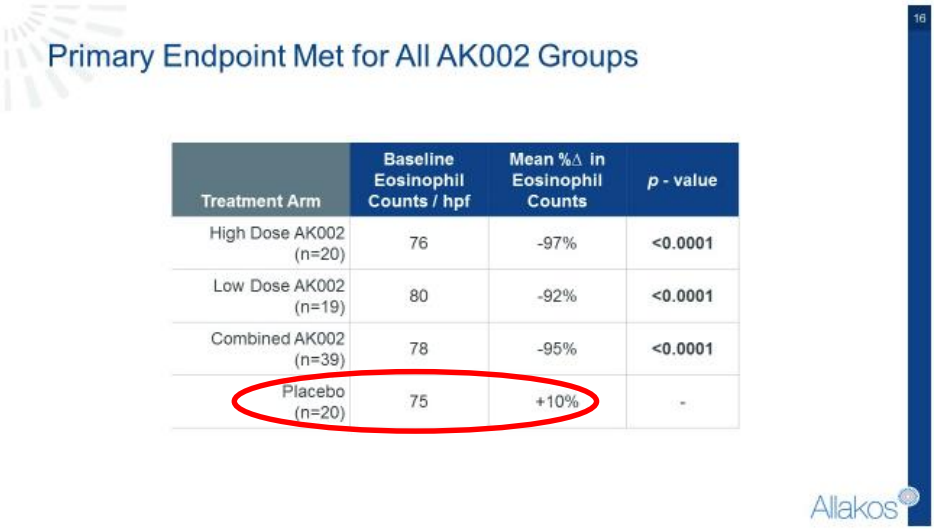
Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	AK002 Dose Groups Low (n=19/12/22)	AK002 Dose Groups High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	ITT	0.0260	0.1556	0.0359	-

Allakos

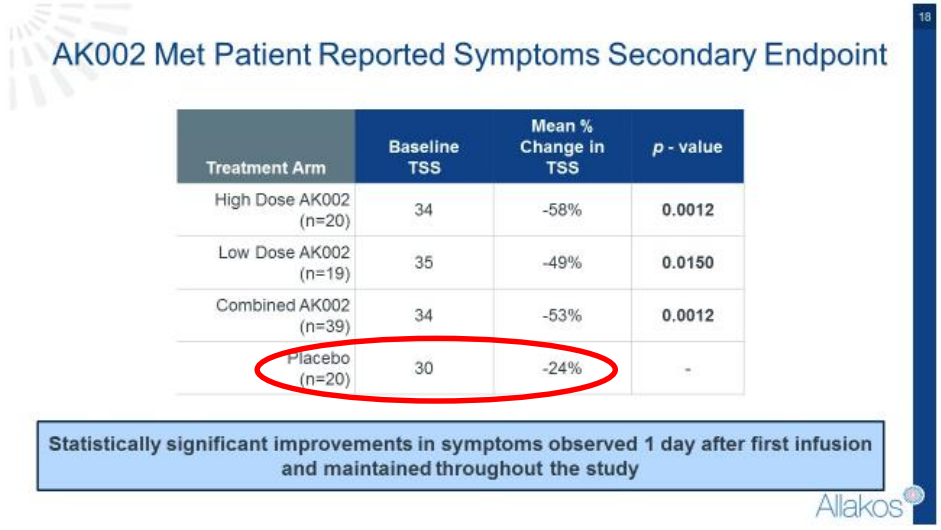
Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #8: Fatal discrepancies and internal contradictions in the ENIGMA data

Further calling the eosinophil thesis into question, Allakos states that eosinophils actually increased by 10% in the placebo group, yet the placebo group symptoms still improved by 24%. We note that the active arm only showed a purported 53% symptom reduction, making a 24% reduction in the placebo arm extremely meaningful by comparison.



Treatment Arm	Baseline Eosinophil Counts / hpf	Mean %Δ in Eosinophil Counts	*p* - value
High Dose AK002 (n=20)	76	-97%	**<0.0001**
Low Dose AK002 (n=19)	80	-92%	**<0.0001**
Combined AK002 (n=39)	78	-95%	**<0.0001**
Placebo (n=20)	75	+10%	-



Treatment Arm	Baseline TSS	Mean % Change in TSS	*p* - value
High Dose AK002 (n=20)	34	-58%	**0.0012**
Low Dose AK002 (n=19)	35	-49%	**0.0150**
Combined AK002 (n=39)	34	-53%	**0.0012**
Placebo (n=20)	30	-24%	-

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #8: Fatal discrepancies and internal contradictions in the ENIGMA data

As another worrisome discrepancy, the p-values suggest that steroids made symptoms worse, which is absurd as steroids are the standard of care and drive symptom improvement in the vast majority of patients. Note the large decline in efficacy between the low dose ITT and "no steroids" groups in total symptom score, from .0313 to .1556. In other words, patients without steroids supposedly improved, but when 10 patients with steroids are added back (i.e., the ITT group), the p-value drops to .1556 and is no longer statistically significant. A similar absurdity is visible in the high dose cohort, which also shows a sharp drop in efficacy when patients on steroids are added back. We cover the role of steroids as a confounding factor in more detail in a later section.

All Analyses Show Consistent Results

Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	AK002 Dose Groups Low (n=19/12/22)	AK002 Dose Groups High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	**<0.0001**	**<0.0001**	**<0.0001**	-
	No Steroids	**<0.0001**	**<0.0001**	**<0.0001**	-
	ITT	**<0.0001**	**<0.0001**	**<0.0001**	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	**0.0009**	**0.0019**	**0.0008**	-
	No Steroids	**<0.0001**	**0.0001**	**<0.0001**	-
	ITT	**0.0008**	**0.0017**	**0.0007**	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	**0.0012**	**0.0150**	**0.0012**	-
	No Steroids	**0.0016**	**0.0313**	**0.0027**	-
	ITT	**0.0260**	0.1556	**0.0359**	-

Allakos

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #8: Fatal discrepancies and internal contradictions in the ENIGMA data

Furthermore, despite n=43 in the active arms, we believe that one or at most two outlier patients swung the symptom improvement p-values into statistical significance. We asked seven different biostatisticians and experts in clinical trial design to analyze Allakos ENIGMA results, including two biostatisticians known for identifying discrepancies and/or fraud in clinical papers, and a third with a specialty in GI trials specifically. Their analyses were unanimous in indicating that the Allakos trial barely scraped over the finish line. We spoke with an ENIGMA trial investigator – a KOL in the space and recipient of payments from Allakos – who affirmed this as possibility.

"It's certainly possible that one patient outlier drive stat sig in the high dose arm. If a couple of people here went in the wrong direction it could sway the p-values." *- ENIGMA trial investigator*

All Analyses Show Consistent Results

Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	AK002 Dose Groups Low (n=19/12/22)	AK002 Dose Groups High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	ITT	0.0260	0.1556	0.0359	-

Allakos

High dose ITT p-value of .026 with n=21 suggests 1-2 patients swung results

Low dose arm failed with p-value of .1556, but even PP and steroid subgroup p-values were only .015 and .0313, respectively, with n=19 and 22.

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; Seligman expert consultation; red ours for emphasis.

Warning sign #8: Fatal discrepancies and internal contradictions in the ENIGMA data

Aside from the ENIGMA investigator, the experts' comments were devastating in describing the role of one or two patients in barely pushing the trial into statistical significance. The statistician particularly renowned for identifying fraud in published medical studies has precipitated the retraction of scores of papers internationally. The other is a professor of biostatistics known for similar analysis. Both were extremely skeptical of Allakos' data and outlined other red flags beyond the impact of an outlier patient. One conducted an analysis to reverse-engineer Allakos' p-values and concluded the published values were not only "incorrect" but off by a factor of 10. The concerns were echoed by a third expert who specializes in trial design and sensitivity/stress tests.

"It's one patient giving them statistical significance. This patient is a huge outlier. *That's quite odd in statistical analysis."* ***– Professor of biostatistics with expertise in uncovering discrepancies in clinical trials***

"The per protocol and ITT p-values are due to a huge outlier. *It's also due to the statistical approach they've proposed. This I believe is based on a student t-test.* ***The data is heavily influenced by the outlier. It's quite rare but mathematically possible in data I've seen to have one outlier create the impact****….Phase 2 data is often risky because of small sample sizes. The chance of one person swinging ITT and per-protocol P-values is smaller with larger sample sizes."* ***– Professor of biostatistics with expertise in uncovering discrepancies in clinical trials***

"The p-values on page 24 can be driven by one outlier. If you had one patient who got a lot worse, it can drive the effect. It's totally possible." ***– Biostatistician with expertise in trial design and GI trials specifically***

"I found it peculiar that the p-values on page 24 [of the Aug 5th ENIGMA results presentation] were ones I could calculate and weren't the same as ones they calculated*. It's possible that it could be some kind of software issue.* ***Some p-values were off by a factor of 10****. I don't understand why there's a discrepancy. I can't tell if it's incompetence or some other reason."* ***– Biostatistics expert known for uncovering fabricated data***

Source: Seligman expert consultations

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Warning sign #8: Fatal discrepancies and internal contradictions in the ENIGMA data

The level of skepticism of the Allakos results was both unanimous and extreme, by every specialist in statistical analysis of clinical trials and researcher/scientist that we engaged to analyze the ENIGMA data.

"The published phase 2 data lacks of anything to get your teeth into. There's not enough data to run any analysis to give you insight into whether the data is reliable*. It's a small study with not much information to go on.* ***It doesn't feel like a frank disclosure.*** *I have three articles sent to me every week. The majority put a spin on the results. On a bit of digging it becomes clear what people have done."* ***– Biostatistics expert known for uncovering fabricated data***

"This data is so sparse. The FDA will have access to a lot more." ***– Research scientist***

*"****There's a lot heterogeneity in the placebo and treatment population****. This is a very diverse group.* ***Then the basic assumptions used for statistical analysis aren't shown. There's not much statistical value here.*** ***I have many concerns about p-values****. The company doesn't specify the statistical test used. They didn't specify the null hypothesis, or the distribution of the test.* ***One can't say anything about the meaning or value of these p-values****."* ***– Professor of mathematics/biostatistics***

"There's a lot of grandstanding in the presentation which makes me uncomfortable." ***– PhD/scientist who conducted due diligence at one of the largest biotech companies***

"A lot of the results Allakos presents weren't planned beforehand. *They're just showing things that support the drug.* ***There's no detail on the all the methods commonly used to limit bias****. It seems reasonable to assume that they had access to patient by patient results.* ***It's just another thing that detracts from showing that the results are a true representation of the drug.*** *They inserted inclusion and exclusion criteria that weren't specified initially.* ***I wonder if they retrospectively applied the inclusion and exclusion criteria."*** *–* ***Biostatistics expert known for uncovering fabricated data***

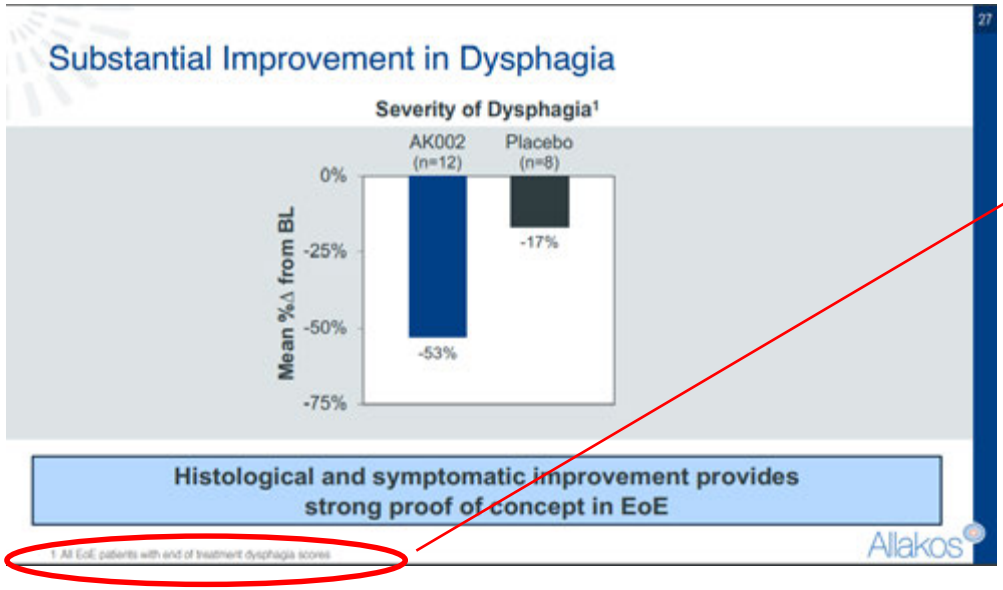
Source: Seligman expert consultations

Warning sign #8: Fatal discrepancies and internal contradictions in the ENIGMA data

Allakos claims that AK002 reduced dysphagia (trouble swallowing) in the EoE subgroup in the EG/EGE trial. Dysphagia is the hallmark symptom of EoE, and therefore Allakos claim is crucial to assess. However, we note yet another discrepancy: Allakos' states unambiguously that their PRO measured only 8 symptoms – EXCLUDING dysphagia - and then the company claims dysphagia reduction anyway in the Aug 5th trial results presentation. Furthermore, despite the company's fascination with p-values over response rates, this page omits p-values altogether - because, we believe, the data is not statistically significant despite bar charts that try to suggest the opposite.

Allakos' Chief Medical Officer comments on Aug 5th call

"Our PRO measures 8 symptoms on a scale from 0 to 10, 10 being the most severe. So the Total Symptom Score is 80 points. So a reduction in Symptom Score is a good thing. ***The 8 symptoms we looked at were: abdominal pain; nausea; vomiting, early satiety, which means fulfillment before ending a meal; the loss of appetite; abdominal cramping; bloating; and/or diarrhea."***



Footnote states "All EoE patients with end of treatment dysphagia scores"

PRO excluded dysphagia, so where are these "dysphagia scores" mysteriously coming from?

Is Allakos being truthful with investors about the composition of their PRO and what symptoms "we looked at"?

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm' CapitalIQ call transcript; red ours for emphasis.

Warning sign #9: Aside from discrepancies, the trial results are compromised by 1) glaring omissions, 2) cherry-picked measures, and 3) statistical gimmicks and obfuscation, making a mockery of standard biotech disclosure and indicative of a trial where all is not as it appears.

1. The top-line readout presented a table of p-values for various subgroups – an unusual format for a critical page – and excluded response rates/percent changes, without which the trial results cannot be evaluated.

2. On other pages where some effect sizes are selectively provided, Allakos again withholds basic data, such as standard deviations, error bars, or the statistical tests used,

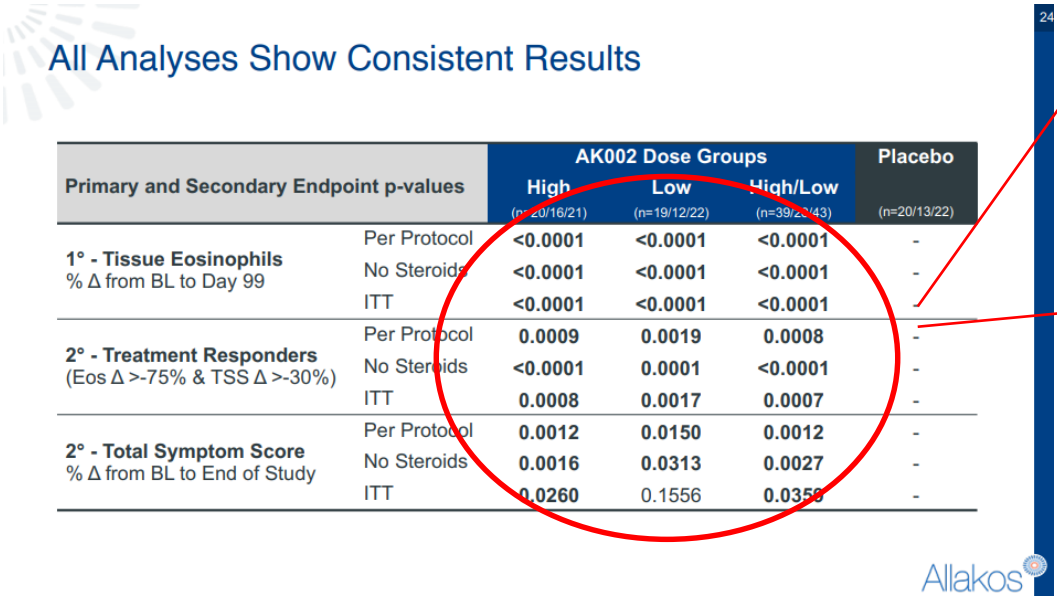
3. The company fails to break out critical data by low and high dose AK002 arms, cherry-picking results by arm on a few pages but lumping them together on critical measures.

4. Virtually every page employs a different statistical measure or gimmick, depending on what casts the data in the best light. The manner in in which p-values appear or disappear from sequential pages is stunning, and we believe, not accidental.

In the words of one scientist we consulted, "It's comparing apples and organs on each slide…The data is cherry-picked and dishonest."

Warning sign #9: Glaring omissions, cherry-picked measures, and statistical gimmicks and obfuscation

In addition to numerous discrepancies, the Aug 5th EG/EGE presentation is marked by surprising omissions that make a parody of standard industry practice. Notably, the table of p-values for various subgroups – an unusual format for a critical page – excluded response rates/percent changes, without which the trial results cannot be evaluated. Investors trying to understand something as basic as AK002's effect on symptoms were left in the dark. We further note the absence of any patient-level data - easy to provide and typically done for trials this small.



Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	Low (n=19/12/22)	High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	ITT	0.0260	0.1556	0.0358	-

"P-values are not informative and no clinician cares. They want to know response rates. The effect sizes are what matters and they don't show them." –
Biostatistician who specializes in clinical trial design and evaluation

"They took the placebo values off this page. There are no p-values shown. This is a problem throughout the deck. ***They obviously have those numbers. I've never seen a table of p-values like this****. Companies show means and standard deviations and show p-values as an asterisk.* ***This is an odd way to show data. And to not show placebo values is strange. It looks to me like they manipulated these numbers to look good. Why didn't they show the data the way it's usually done?"***
- PhD/scientist who previously conducted due diligence at one of the largest biotech companies

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm' red ours for emphasis.

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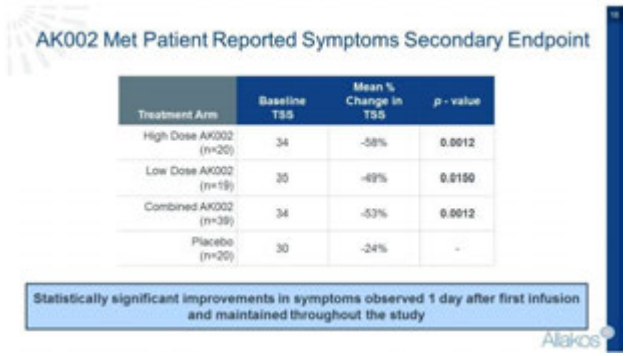
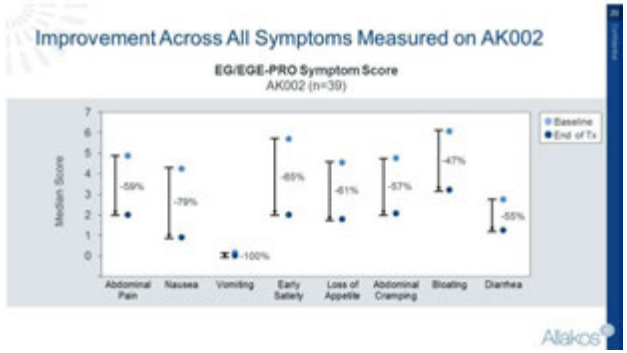
Warning sign #9: Glaring omissions, cherry-picked measures, and statistical gimmicks and obfuscation

On pages where some effect sizes are selectively provided, Allakos again withholds basic, industry-standard data, making one wonder what the company may be trying to hide. We asked five biostatisticians, scientists, and trial design experts to assess each slide in the Aug 5th EG/EGE top line read-out. The skepticism from one expert below is representative.





→ *"Companies usually have plus/minus standard deviation which allows you to back into and calculate what's going on.* ***It's a red flag.*** *Normally those are put in.* ***We have no idea how wide the distribution is around the mean. Their not showing standard deviation is a big deal."***

→ ***"There's no standard deviation and no p-value shown for the placebo effect.*** *Companies usually compare dose groups to placebo directly.* ***If it wasn't statistically significant, they'd put the p-value in there. It's so easy to do****. Look at percent change by patients compared to percent change in the patients and see if its stat sig.* ***This data isn't conclusive without that information."***

→ ***"There's no graph of Total Symptom Score. This page just combines everything and doesn't separate low/high dose, placebo, steroids, no steroids****. It also only shows the median, without showing mean and standard deviation.* ***They're trying to make data look as good as they can without giving a lot of info****. Allakos doesn't say what kind of statistical test they use to calculate the p-values…Nothing in the materials tells you."*

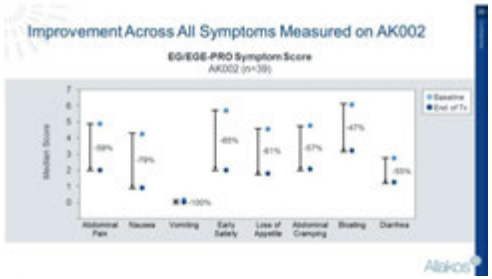
- PhD/scientist who conducted due diligence at one of the largest biotech's

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm

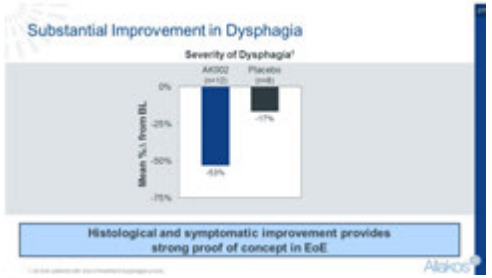
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #9: Glaring omissions, cherry-picked measures, and statistical gimmicks and obfuscation

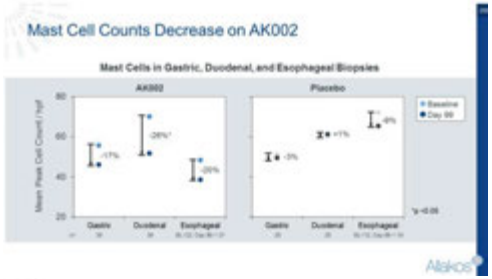
The company's failure to break out critical data by low and high dose AK002 arms continues the pattern of cherry-picking and omissions. Allakos breaks out results by arm on a few pages, and then proceeds to lump the arms together on critical measures. We note four crucial claims where Allakos reticence to separate data by arm is suspect.



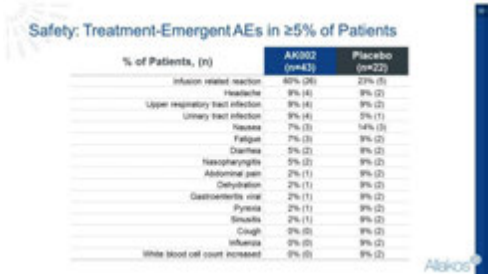
→ ***PRO Symptom Scores:*** *we find it stunning that Allakos failed to share how each dose affected the various symptoms measured.*



→ ***Reduction in severity of dysphagia:*** *as the defining symptom of EoE, the lack of data by arm renders the minimal EoE data shared on Aug 5th even less relevant or informative.*



→ ***Mast cell counts decrease:*** *mast cells, which express Siglec-8, are core to the AK002 Siglec8-inhibition story. The data is already dubious, as it indicates that AK002 flopped in showing statistical significance in two of three biopsy measures. Only the duodenal count showed stat sig, yet Allakos bizarrely only provides one p-value and fails to state which arm it applies to.*



→ ***Adverse events:*** *in yet another departure from industry-standard disclosure norms, Allakos prevents investors from understanding the relationship between dose level and safety. Warning signs related to this signal have blown up many biotech companies.*

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm

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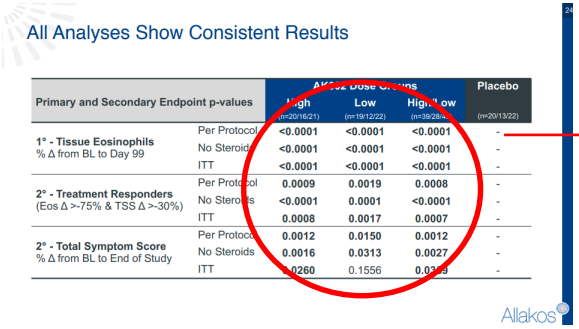
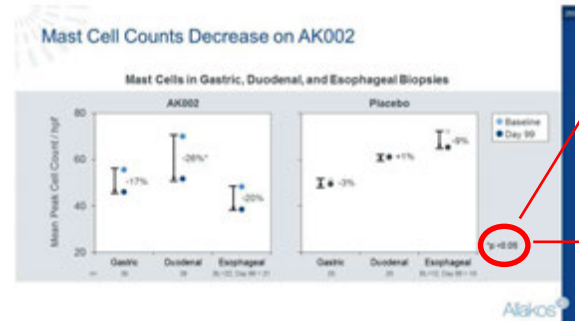
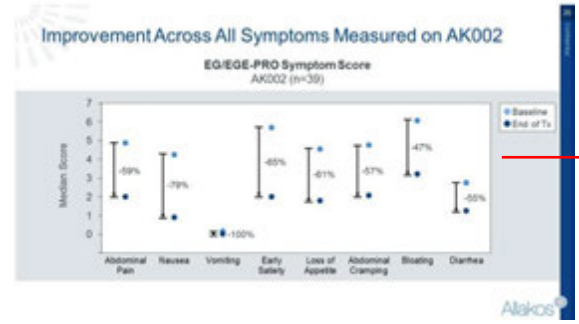
Warning sign #9: Glaring omissions, cherry-picked measures, and statistical gimmicks and obfuscation

The preceding examples of discrepancies, omissions, and cherry-picking suggest to us a company that is not playing it straight with investors. Virtually every page employs a different statistical gimmick in an attempt - we believe - to mislead investors. None of this would fly with credible medical journals – much less the FDA – and explains the conspicuous lack of validation and peer review. In particular, we note the company's selective and inconsistent fascination with p-values.







A critical table in the top-line readout is all p-values vs. standard practice of showing response rates/effect size.

Yet, other key charts such as on mast cell reduction omit p-values and show effect size instead, because – as revealed by a tiny asterisk – the p-values are not stat sig for 2 of 3 measures.

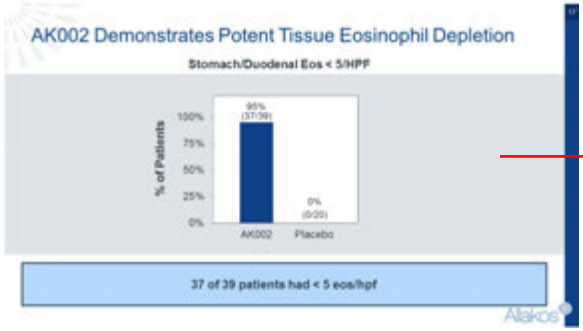
Why is the p-value suddenly shown as a threshold value ("p<.05") when the table above shows them to four significant digits? The threshold for statistical significance is .05, and this suggests the p-value is barely below .05 – technically statistically significant but irrelevant, and a red flag for data manipulation.

Why is a p-values table missing completely on the crucial symptoms improvement chart?

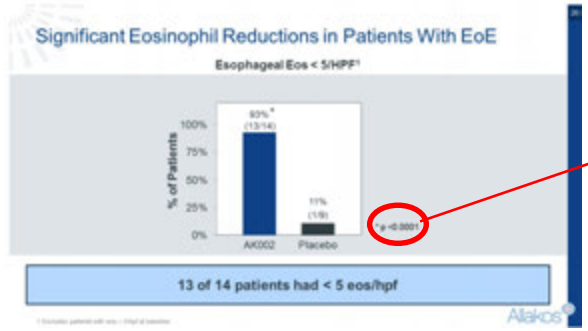
Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #9: Glaring omissions, cherry-picked measures, and statistical gimmicks and obfuscation

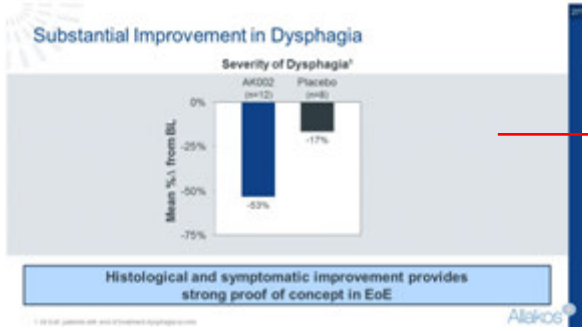
The manner in which p-values appear or disappear from sequential pages is stunning, and we believe, not accidental. The lack of error bars, standard deviations, and other standard information is unusual. In the words of one scientist we consulted, "It's comparing apples and organs on each slide…The data is cherry picked and dishonest."



Slide 17 says AK002 shows "potent tissue eosinophil depletion", yet the p-value is conspicuously absent.



Slide 26 claims "significant eosinophil reductions" in EoE patients and a statistically significant p-value suddenly re-appears.



Yet the very next slide claiming "substantial improvement in dysphagia" – the defining symptom of EoE – reverts back to omitting the p-value. The only conclusion we can draw from the lack of a p-value is that AK002 is a dud when it comes to the most important symptom of EoE.

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #10: Since the superficial ENIGMA release on Aug 5th, Allakos has yet to follow up with proper data at a medical conference or in a peer-reviewed publication, which we find alarming relative to standard practice. The company has had three key opportunities to fill in gaping holes and failed to do so. The scraps of additional data which have been shared raise more questions than answers, with red flags beyond those in the Aug 5th package. Alarmingly, critical information from Aug 5th – such as p-values – keeps shifting, suggesting a lack of data integrity, incompetence, or worse. Further, the Aug 5th presentation appears to have now been deleted from the Allakos site, replaced by one less than half the length and missing key data in the original.

The company has had three marquee opportunities to fill in the gaping holes and selective disclosures from the August 5th readout, and failed to do so: 1) an October 22 presentation at a key European GI conference, United Gastroenterology Week in Barcelona; 2) an October 29 presentation at the American College of Gastroenterology meeting in San Antonio; 3) a November 8 presentation at the CURED EGID conference in Cincinnati.

We find it surprising that critical data has changed since the topline results on Aug 5th. As Allakos has not disclosed any errors to investors, the changes strike us as clearly intentional:

1. **There are now 5 versions of the critical slide on eosinophil depletion in stomach/duodenal tissue, with different combinations of p-values and other data.**

2. **The data for eosinophil depletion in esophageal tissue in the EoE subgroup has also shifted.**

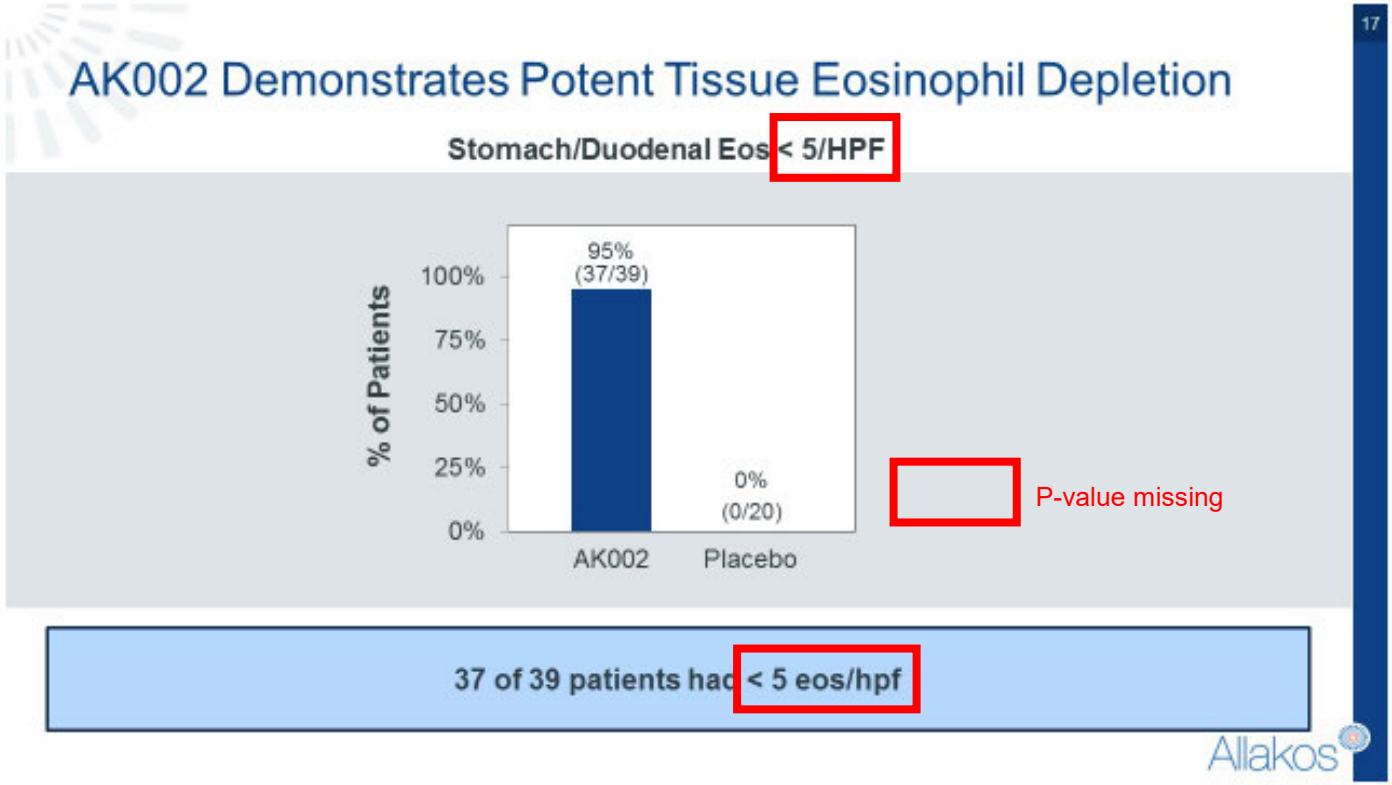
Warning sign #10 (cont'd): Still no proper data since topline readout, scraps of new data raise troubling questions

3. An alarming footnote has been added to the baseline characteristics slide from August 5th, suggesting that Allakos used an artificial baseline from which to measure eosinophil and mast cell reductions – the single site with the highest count versus an average of several biopsies per typical practice and FDA guidance.

Warning sign #10: Still no proper data since topline readout, scraps of new data raise troubling questions

We begin by noting red flags in the ENIGMA trial primary endpoint slide on tissue eosinophil depletion, shown below from the August 5th top-line results. Different versions of this crucial slide have been presented FOUR times after the original release, on 1) Oct 22 at UEG in Barcelona, 2) October 29 at ACG in San Antonio, 3) November 8 at the CURED conference in Cincinnati, and alarmingly 4) in a "revised version" of the November 8 slide which conference organizers send to attendees a couple of weeks after. We highlight the sections which dance around, notably the 1) the definition of HPF (high power field), 2) the p-value (missing in the slide below), and 3) eosinophil reduction.

Original August 5th version from ENIGMA read-out

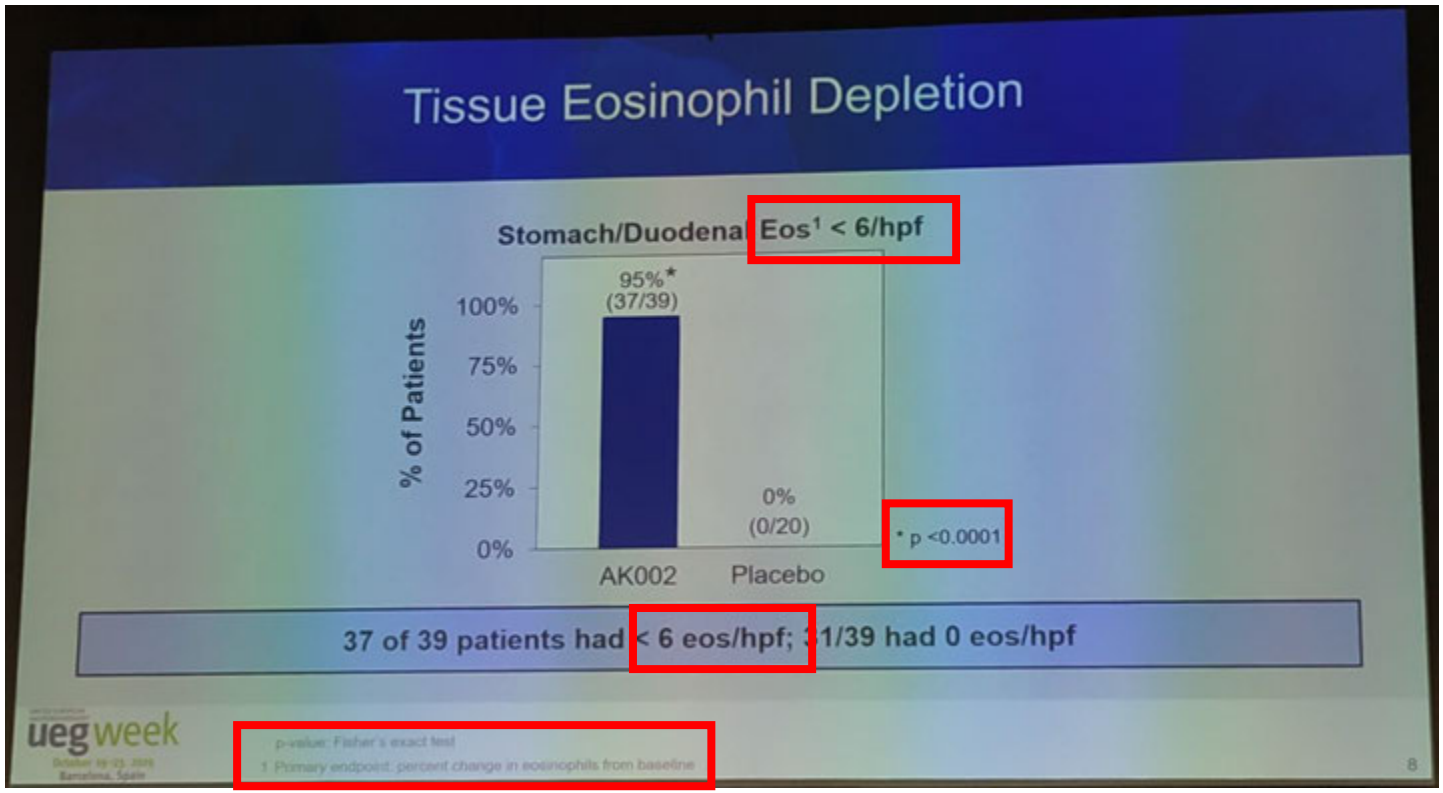


Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #10: Still no proper data since topline readout, scraps of new data raise troubling questions

The version of the primary endpoint slide subsequently presented on October 22 in Barcelona fails to match the August 5th. The definition of HPF at top is changed from "<5" to "<6". A p-value suddenly appears. Eosinophil reduction at the bottom is also changed from "<5 eos/hpf" to "<6 eos/hpf". Two details are added as footnotes. One qualifies the stomach/duodenal eosinophil reduction as "Primary endpoint percent change in eosinophils from baseline" and the other specifies a statistical test ("p-value: Fisher's exact test").

October 22/Barcelona version of primary endpoint slide

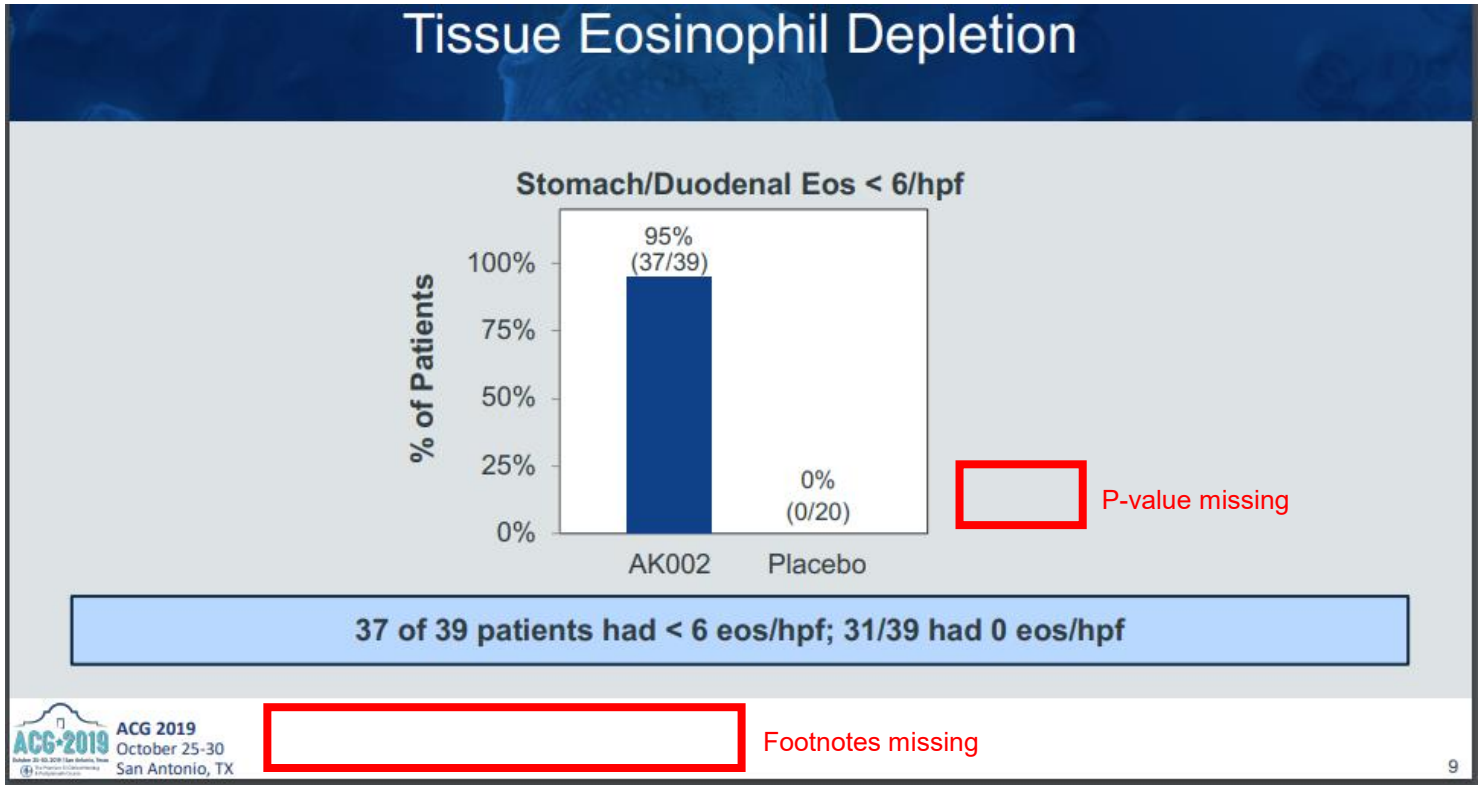


Source: UEG Week 2019 presentation: "Efficacy and Safety of AK002 in Adult Patients With Active Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis: Primary Results From a Randomized, Double-Blind Placebo-Controlled Phase 2 Trial (ENIGMA Study)", https://acgmeetings.gi.org/wp-content/uploads/2019/10/ACG2019_Final-Program.pdf p.64; red ours for emphasis.

Warning sign #10: Still no proper data since topline readout, scraps of new data raise troubling questions

The October 22 version changes again a week later in San Antonio, representing the THIRD version of this crucial slide. The p-value is now removed as are the footnotes. Given that Allakos has not disclosed any data errors and the presenter, the additions and removals strike us as clearly deliberate.

October 29/San Antonio version, one week after UEG

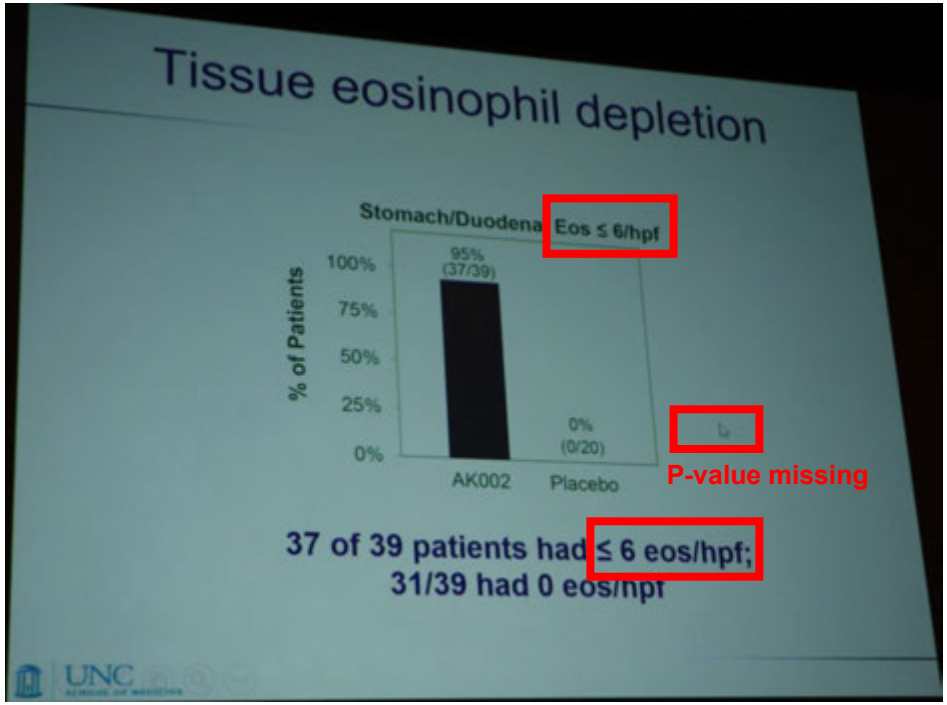


Source: ACG presentation on ALLK IR site http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; red ours for emphasis.

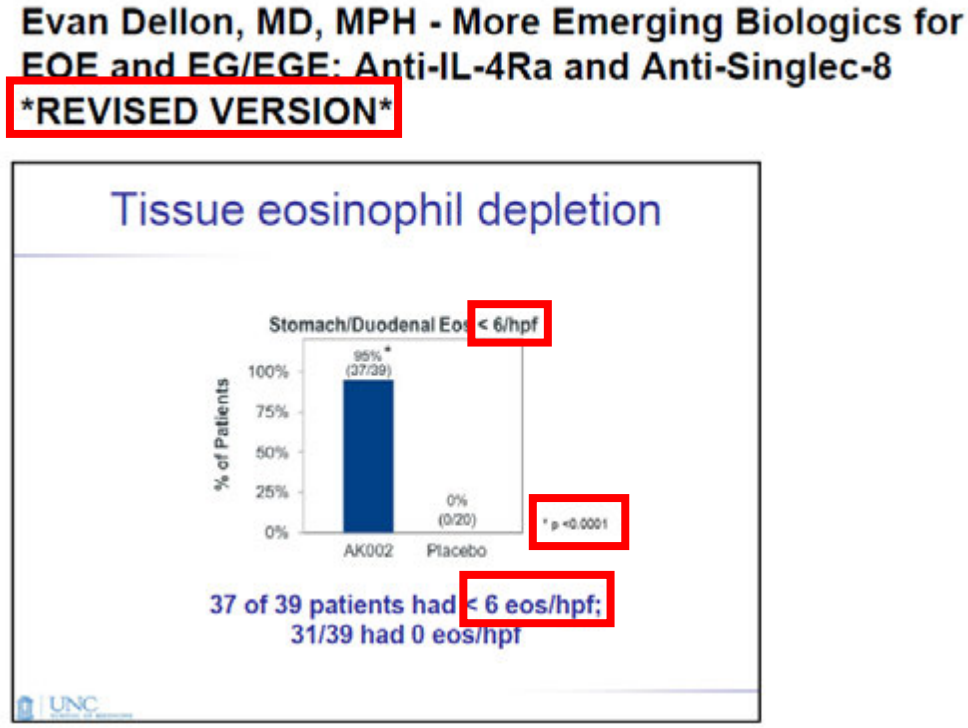
Warning sign #10: Still no proper data since topline readout, scraps of new data raise troubling questions

The Cincinnati version the Principal Investigator presents on Nov 8 marks the FOURTH version. We now see an entirely new definition of HPF at top and of eosinophil reduction at bottom: "≤6/HPF" versus "<5" and "<6" before. This was followed by a FIFTH iteration when conference organizers sent a revised version to attendees a couple of weeks after. The definitions are changed back to "<6" and with a p-value re-inserted. Investors should be asking why the definition of the primary endpoint keeps changing from week to week, much less why the principal investigator and/or conference took the remarkable step of issuing what looks like a retraction.

November 8/Cincinnati version



"Revised version" of Cincinnati sent after conference

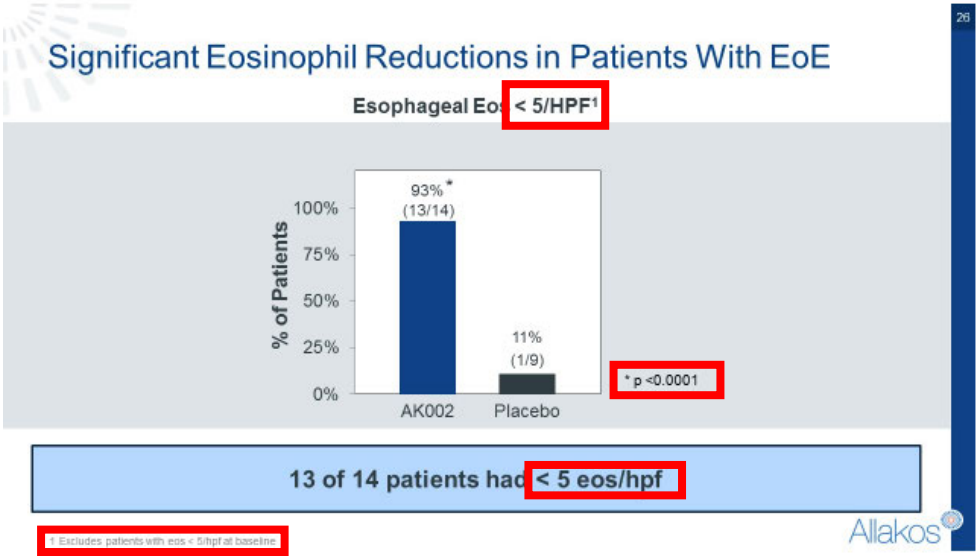


Source: "Fifth CURED EGID Research Conference" presentation" by Evan Dellon, https://www.regonline.com/custImages/460000/465951/2019CUREDAgendawithSpaces.pdf;; CURED conference organizers; red ours for emphasis.

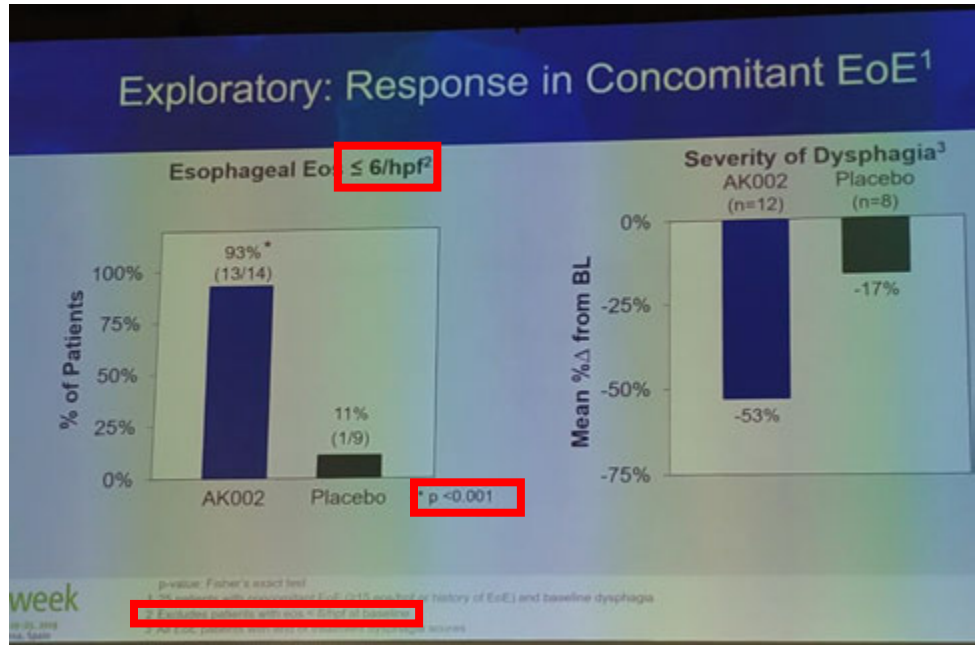
Warning sign #10: Still no proper data since topline readout, scraps of new data raise troubling questions

The new information presented since the August 5th presentation is notable not only for shifting definitions of the eosinophil endpoint in EG/EGE (stomach/duodenal tissue) but also for a similarly shifting definition of eosinophil reduction in the EoE subgroup (esophageal tissue) – a worrisome issue for investors given its importance as an endpoint in any prospective EoE trial. The EoE endpoint changes from <5/HPF on Aug 5th to ≤6/HPF at UEG on Oct 22, as does the criteria in the footnote for excluding patients from the measurement. The p-value changes from <..0001 to <.001, a 10X worsening. When asked during the ACG Q&A, the PI claimed it was a typo, which makes no sense given that the definition of HPF was altered as well.

Original August 5th version from ENIGMA read-out



October 22/Barcelona version

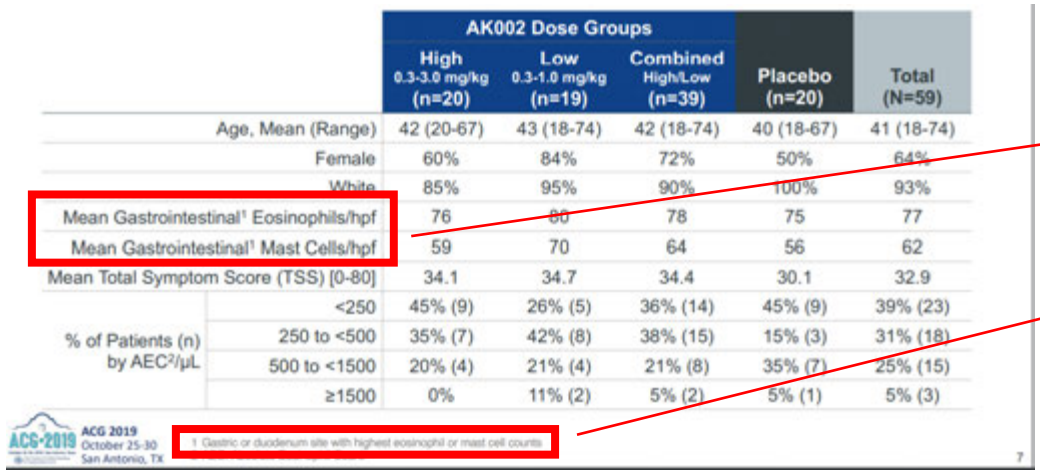


Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; UEG Week 2019 presentation: "Efficacy and Safety of AK002 in Adult Patients With Active Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis: Primary Results From a Randomized, Double-Blind Placebo-Controlled Phase 2 Trial (ENIGMA Study)", https://acgmeetings.gi.org/wp-content/uploads/2019/10/ACG2019_Final-Program.pdf p.64; red ours for emphasis.

Warning sign #10: Still no proper data since topline readout, scraps of new data raise troubling questions

The October 29th ACG version of the ENIGMA results presentation also changed the baseline characteristics slide first presented on August 5th. A footnote is added to qualify the starting mean eosinophil and mast cell counts in tissue, stating "Gastric or duodenal site with highest eosinophil or mast cell counts". Cells counts via microscope HPF by a pathologist are unreliable given the irregular distribution of eosinophils and mast cells in the stomach or duodenum. The FDA expects counts averaged over multiple biopsies, and best practice uses multiple pathologists to limit bias. ENIGMA trial investigators told us that the trial used only one pathologist, who we noted earlier disclosed a conflict of interest with Allakos. The new footnote suggests that Allakos used an artificial baseline from which to measure eosinophil and mast cell reductions – the single site with the highest count. Allakos has no footnote explaining how they measure the ending count, and we can only wonder if they cherry-pick the site with the lowest count. We note one of their own investigator's skepticism.

"All these diseases have spontaneity. It's hit or miss measuring cell counts via biopsy. You can be 10 centimeters too close or too far, or 10 minutes too late or too early given their intraday variation. Biopsies here are a hard one." – Allakos trial investigator and KOL



		AK002 Dose Groups				
		High 0.3-3.0 mg/kg (n=20)	Low 0.3-1.0 mg/kg (n=19)	Combined High/Low (n=39)	Placebo (n=20)	Total (N=59)
Age, Mean (Range)		42 (20-67)	43 (18-74)	42 (18-74)	40 (18-67)	41 (18-74)
Female		60%	84%	72%	50%	64%
White		85%	95%	90%	100%	93%
Mean Gastrointestinal[1] Eosinophils/hpf		76	80	78	75	77
Mean Gastrointestinal[1] Mast Cells/hpf		59	70	64	56	62
Mean Total Symptom Score (TSS) [0-80]		34.1	34.7	34.4	30.1	32.9
% of Patients (n) by AEC²/µL	<250	45% (9)	26% (5)	36% (14)	45% (9)	39% (23)
	250 to <500	35% (7)	42% (8)	38% (15)	15% (3)	31% (18)
	500 to <1500	20% (4)	21% (4)	21% (8)	35% (7)	25% (15)
	≥1500	0%	11% (2)	5% (2)	5% (1)	5% (3)

ACG 2019 October 25-30 San Antonio, TX

1 Gastric or duodenum site with highest eosinophil or mast cell counts

Baseline definition states *"Mean Gastrointestinal[1] Eosinophils/hpf"* and *"Mean Gastrointestinal[1] Mast Cell/hpf"*

Footnote states "[1]*Gastric or duodenal site with highest eosinophil or mast cell counts"*

Source: ACG presentation on ALLK IR site http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; red ours for emphasis.

Warning sign #11: Aside from shifting and instable p-values, the incremental data shared since Aug 5th is troubling for other reasons. The only real attempt at filling in gaps is a new slide with PRO response rates over time. However, the curves demonstrate that the response rates are flimsy and clinically irrelevant, strain credibility on other counts, and expose new discrepancies and contradictions that further undermine the ENIGMA results and cast doubt on the company's conduct.

1. The response rates are flimsy and driven by the arbitrary definition of a responder as a patient with ">30% benefit in Total Symptom Score," rendering the trial results a strained statistical artifact. Simple stress tests that tweak the responder definition – as the FDA does in PRO trials – suggest the results easily collapse.

2. Aside from being precarious, the response rates lack clinical relevance as they indicate that patients barely felt better relative to placebo.

3. The response curves strain credibility and fail the too-good-to-be-true test. The AK002 curve indicates a battery of 8 different PRO symptoms plummeting within one to three days – which we find absurd given that patients suffer from GI lesions, tissue masses, edema, and inflammation from years or decades of chronic disease.

4. The curves show a worsening of PRO symptoms in the placebo arm in the final week – a rather lucky and abrupt reversal of trend without which, we believe, the trial would have failed. We doubt this type of data will pass muster with the FDA.

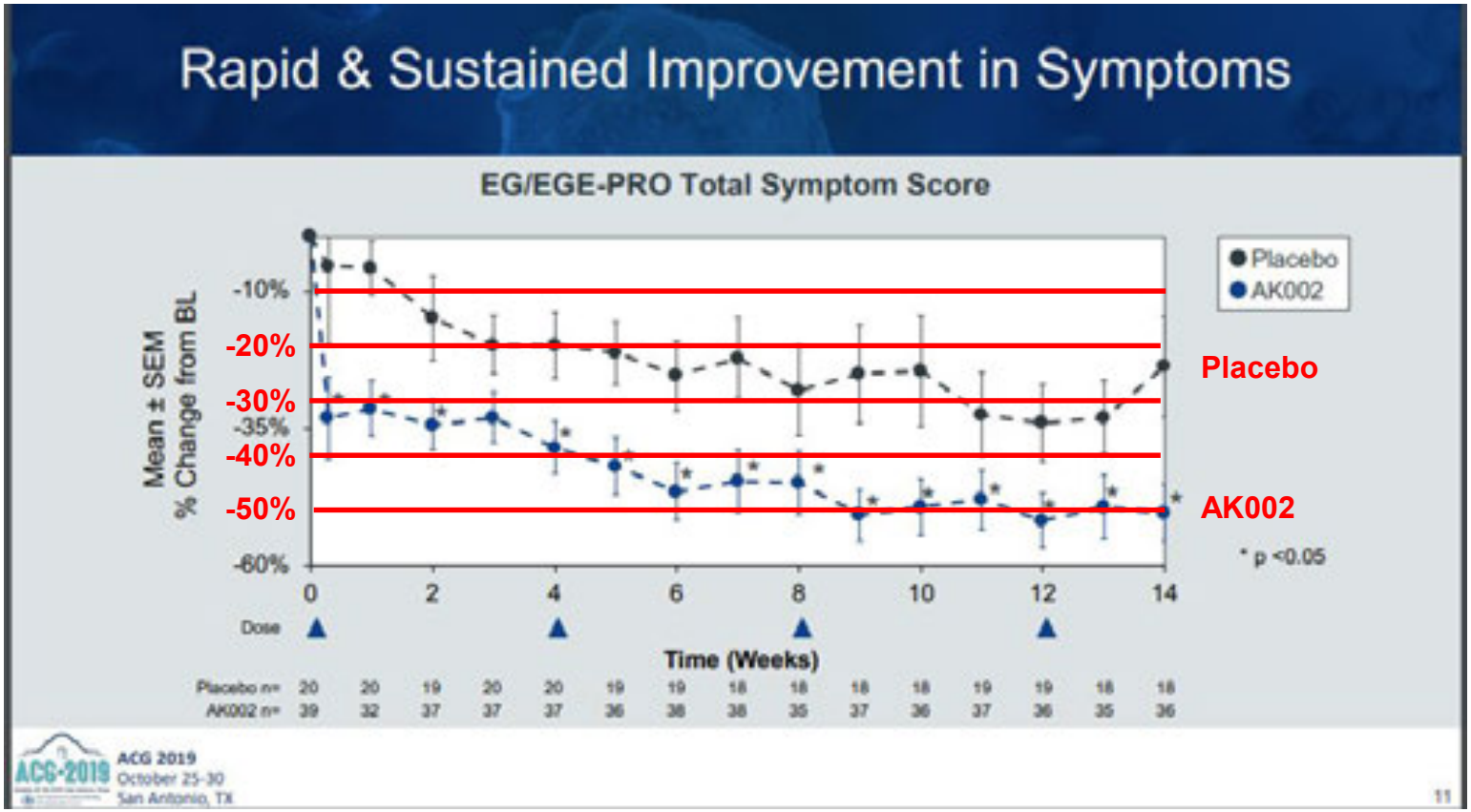
Warning sign #11 (cont'd): Aside from shifting and instable p-values, the incremental data shared since Aug 5th is troubling for other reasons.

5. The response curve clearly indicates that the lowest dose of AK002 (0.3 mg/kg) drove most of the benefit, yet the company dropped the lowest dose going forward – yet another discrepancy and contradiction that undermines the company's credibility.

6. Allakos broke out response rates for each of the 8 symptoms measured in the PRO, although not over time nor broken out by arm. Irrespective, the data exhibits statistically suspect clustering, and fails to match data from August 5th.

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

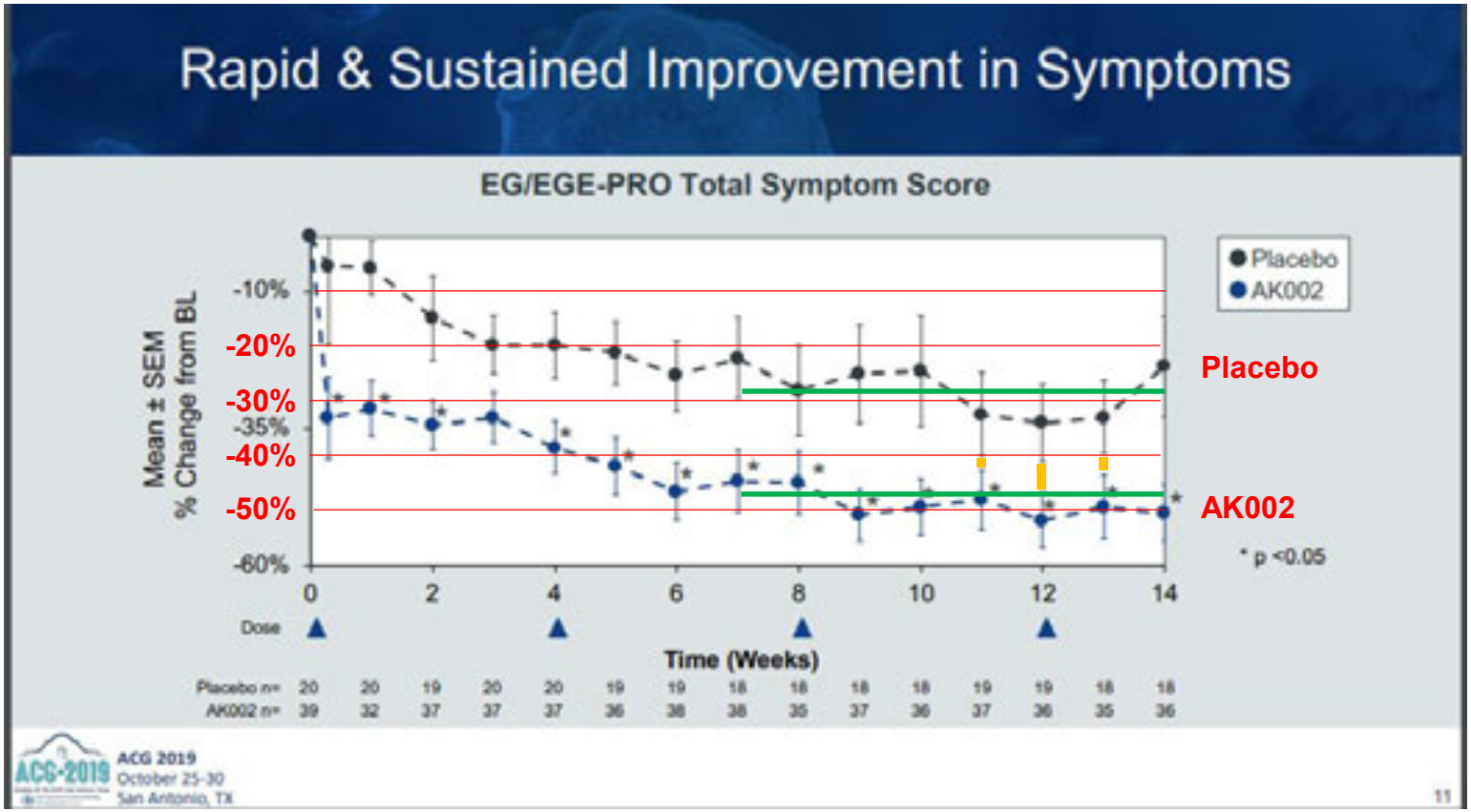
The UEG and ACG presentations showed some scraps of response rate data for PRO Total Symptom Scores, missing on August 5th. We find it interesting that Allakos declined to break out the curves by low and high dose arms. The data is troubling for other reasons. The ENIGMA endpoint arbitrarily defined a responder as a patient with ">30% benefit in Total Symptom Score". The data show that the results are a precarious statistical artifact driven by the 30% definition. Red lines we add below indicate that tweaking the responder definition to 40% or better reduction would have led to trial failure. The FDA does stress tests to ensure that nudging the responder definition in a PRO trial still shows separation between drug and placebo. We see peril with the FDA given how easily the results collapse.



Source: ACG presentation on ALLK IR site http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; red ours for emphasis.

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

Aside from being flimsy, the response rates lack clinical relevance. In the back half of the period below, placebo patients improved by about 30% and AK002 patients improved by about 45% (green lines added to show average). A roughly 15% improvement – and from a flawed, unvalidated PRO with blinding, steroid, and other massive problems – means patients barely feel better. The error bars in later weeks suggest even smaller improvement (orange added between bars). Moreover, PRO's have a margin of error which Allakos has yet to disclose. If this is the most improvement that Allakos can show, despite numerous red flags which in our opinion suggest manipulation, the actual real-world PRO improvement could easily be zero.

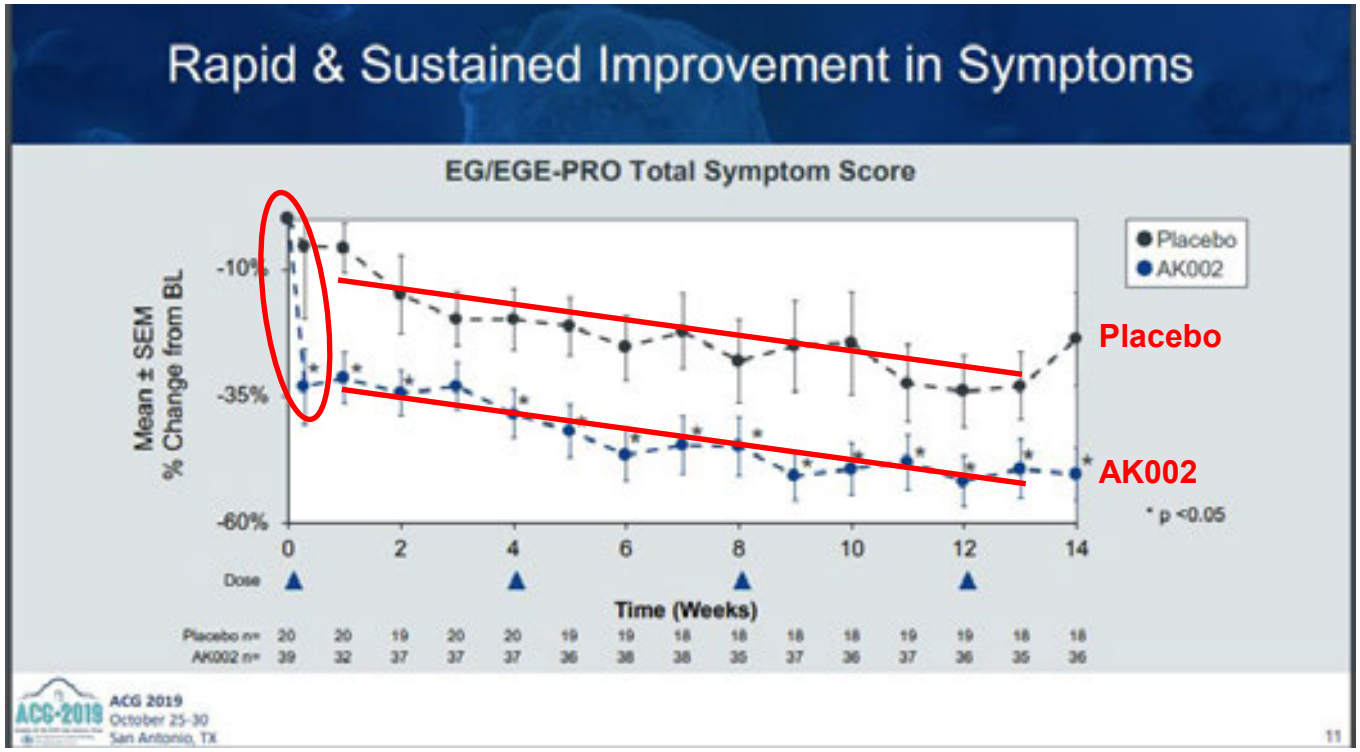


Source: ACG presentation on ALLK IR site http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; red, green, yellow ours for emphasis.

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

The number of other red flags in the AK002 response rate data is astonishing. Patients suffer from GI lesions like submucosal tumors, tissue masses like granules, edema, and inflammation from years or decades of chronic disease. Yet the AK002 curve indicates a battery of 8 different PRO symptoms plummeting within ONE TO THREE days – straining credibility and failing the too-good-to-be-true smell test. AK002 then simply tracks the placebo's path for the rest of the measurement period, reinforcing that most of the purported AK002 symptom benefit over placebo happens instantaneously.

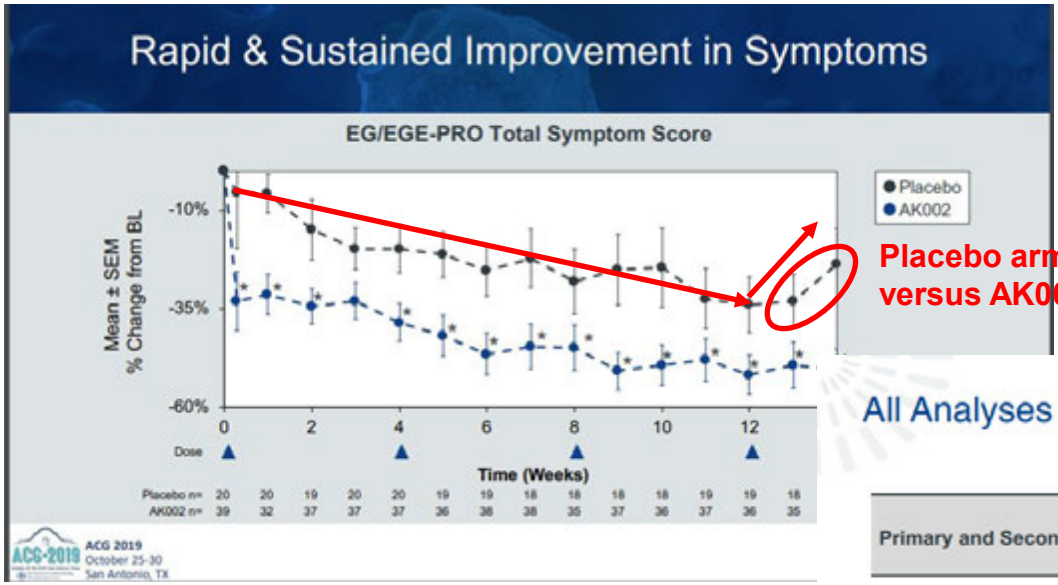
"Also importantly, the effect was almost instantaneously [sic], as we saw statistically significant improvements in symptoms within 1 day of the first infusion." – Allakos Chief Medical Officer, Aug 5th ENIGMA results call



Source: ACG presentation on ALLK IR site http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; CapitalIQ transcript; red ours for emphasis.

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

We further note the worsening of PRO symptoms in the placebo arm in the final week – a rather lucky and abrupt reversal of trend. Recall that p-values for Total Symptom Scores flopped in the low dose arm, and were barely statistically significant in the high and combined dose arms on ITT. Without the convenient boost from the large decline in placebo scores in the final week, it is difficult to see how all arms wouldn't have failed. We wonder how the FDA will feel in phase 3 if "lightning" strikes the same tree twice.



Placebo arm suddenly degrades versus AK002 in final week

All Analyses Show Consistent Results

Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	AK002 Dose Groups Low (n=19/12/22)	AK002 Dose Groups High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	ITT	0.0260	0.1556	0.0359	-

Low does failed to show stat sig and high dose barely scraped over the finish line.

Allakos

Source: ACG presentation on ALLK IR site http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

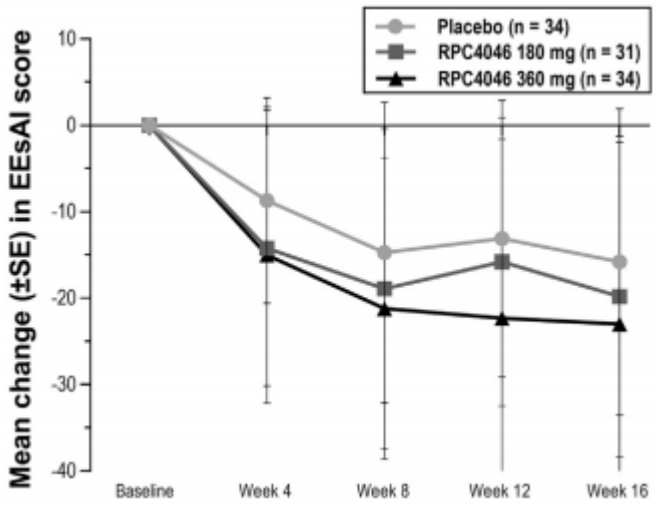
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

Both the clinical literature and competing trials suggest that the AK002 response rate curve is an anomaly that makes no sense, such as a 2019 paper authored by multiple ENIGMA trial investigators including principal investigator Evan Dellon. The first curve shows symptom reduction using a validated EoE PRO. Symptoms require at least 4 weeks to improve. Consistent with common sense, there is no magical drop within days, nor a sudden reversal at the end. The second paper reinforces the trajectory of typical PRO response curves and the absurdity of the Allakos data.

RPC4046, a Monoclonal Antibody Against IL13, Reduces Histologic and Endoscopic Activity in Patients With Eosinophilic Esophagitis

Ikuo Hirano,[1] Margaret H. Collins,[2] Yehudith Assouline-Dayan,[3] Larry Evans,[4] Sandeep Gupta,[5] Alain M. Schoepfer,[6] Alex Straumann,[7] Ekaterina Safroneeva,[8] Michael Grimm,[9] Heather Smith,[9] Cindy-ann Tompkins,[9] Amy Woo,[9] Robert Peach,[9] Paul Frohna,[9] Sheila Gujrathi,[9] Darryl N. Penenberg,[9] Caiyan Li,[9] Gregory J. Opiteck,[9] Allan Olson,[9] Richard Aranda,[9] Marc E. Rothenberg,[2] and Evan S. Dellon,[10] for the HEROES Study Group



Latest Insights on the Relationship Between Symptoms and Biologic Findings in Adults with Eosinophilic Esophagitis

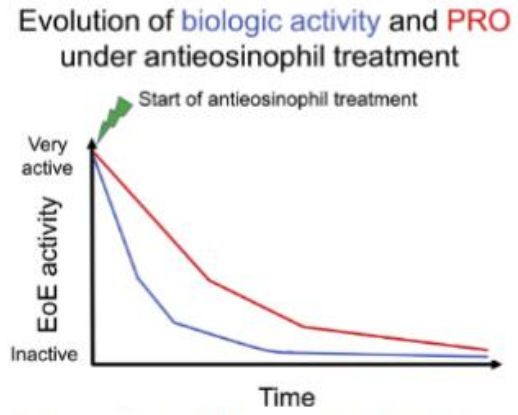
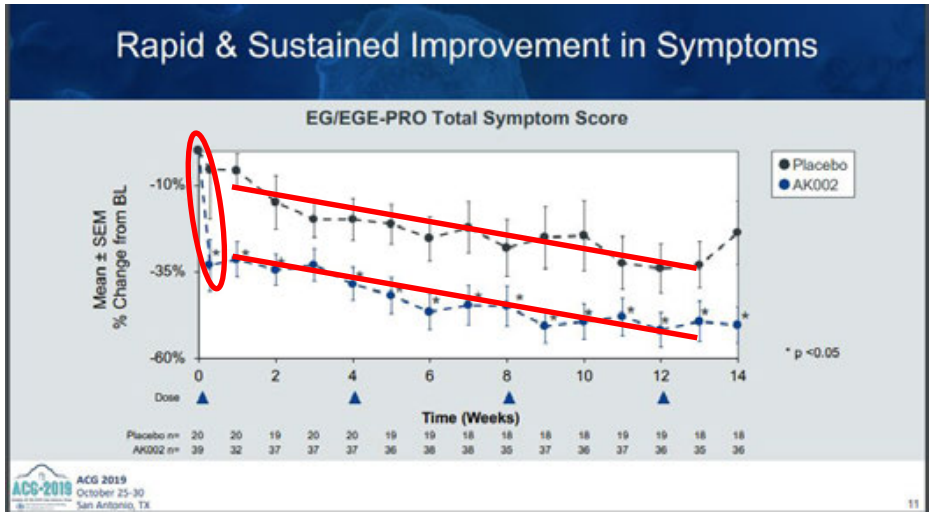


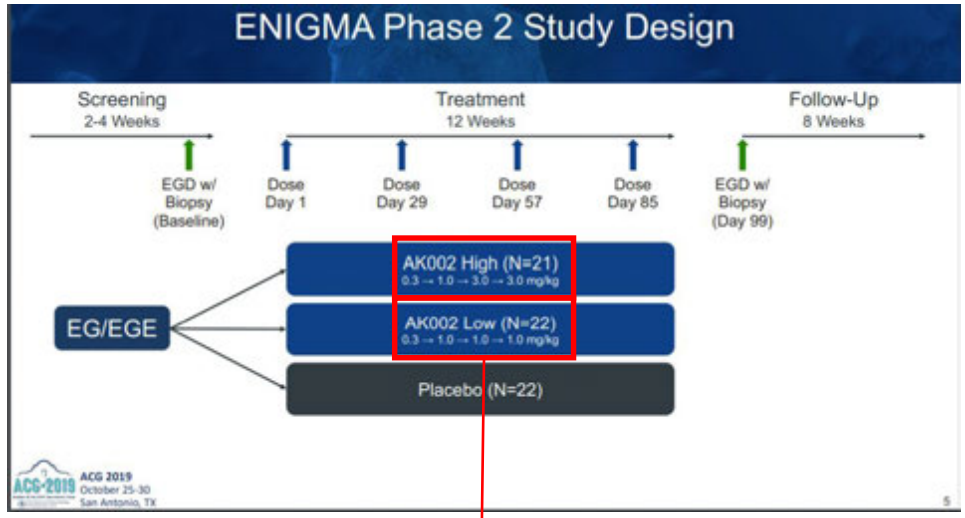
Fig. 2. On introduction of an antieosinophil treatment, biologic activity (endoscopy and histology) tends to improve quicker than symptoms. Thus, clinical studies should evaluate PRO for a sufficient amount of time if PRO improvement is targeted as a study endpoint.

Source: https://www.gastrojournal.org/article/S0016-5085(18)35208-9/fulltext?referrer=https%3A%2F%2Fwww.ncbi.nlm.nih.gov%2F; https://www.sciencedirect.com/science/article/pii/S1052515717300934

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

Just when one thinks Allakos could not have packed more discrepancies and red flags into one slide, we highlight another preposterous example. The response curve, as already noted, indicates that most of the symptom benefit over placebo occurred in the first few days. Yet, the first AK002 dose in both the low and high dose arms was the lowest in the protocol (0.3 mg/kg). The next dose of 1.0 mg/kg wasn't infused until a month later, well after the bulk of the symptom improvement already occurred. This clearly indicates that the lowest dose of AK002 (0.3 mg/kg) drove most of the benefit – which we know cannot be true. We examine Allakos' own statements and another key fact…





High dose infusion schedule from months 1-4: 0.3 – 1.0 – 3.0 – 3.0 mg/kg

Low dose infusion schedule from months 1-4: 0.3 – 1.0 – 1.0 – 1.0 mg/kg

Source: ACG presentation on ALLK IR site http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; red ours for emphasis.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

First, the low dose arm failed to show statistically significant symptom improvement, which contradicts the data in the response curve – which indicates that the lowest dose drove "the magic." Second, comments by both the CEO and Chief Medical Officer during the August 5th ENIGMA top-line results call suggested that the lower dose was insufficient. The CMO indicated that the 0.3 mg dose was being bypassed in the ENIGMA extension study. The CEO expressed uncertainty on whether even 1mg (>3x the lowest dose) was sufficient, and appeared gung-ho on using 3mg/kg (or 10x the dose that the response curve indicates drove most of the benefit). The company has further modified the extension study to allow even higher doses of steroids, to prevent infusion-related reactions and enable administration of the highest AK002 doses they can get away with. Investors should ask, if the low dose drove the symptom benefit - in days, per the response curve – why did they drop it, risking adverse events with higher doses and necessitating even more steroids?

Comments on August 5, 2019, ENIGMA trial results calls

"So what we have introduced in the extension study *now is pre-dosing with oral prednisone 1 day prior to the first and the second AK002 doses […]* ***That has also allowed us to bypass the 0.3 mg/kg starting dose and actually go straight into a 1 mg/kg starting dose."*** *– Allakos Chief Medical Officer*

"So I think it's safe to say that the 3 mg/kg dose is going into Phase III. I think the question we're still debating is whether or not we would put the 1 mg/kg in." *– Allakos CEO*

Low dose arm failed to show symptom improvement with P-value of .1556

All Analyses Show Consistent Results

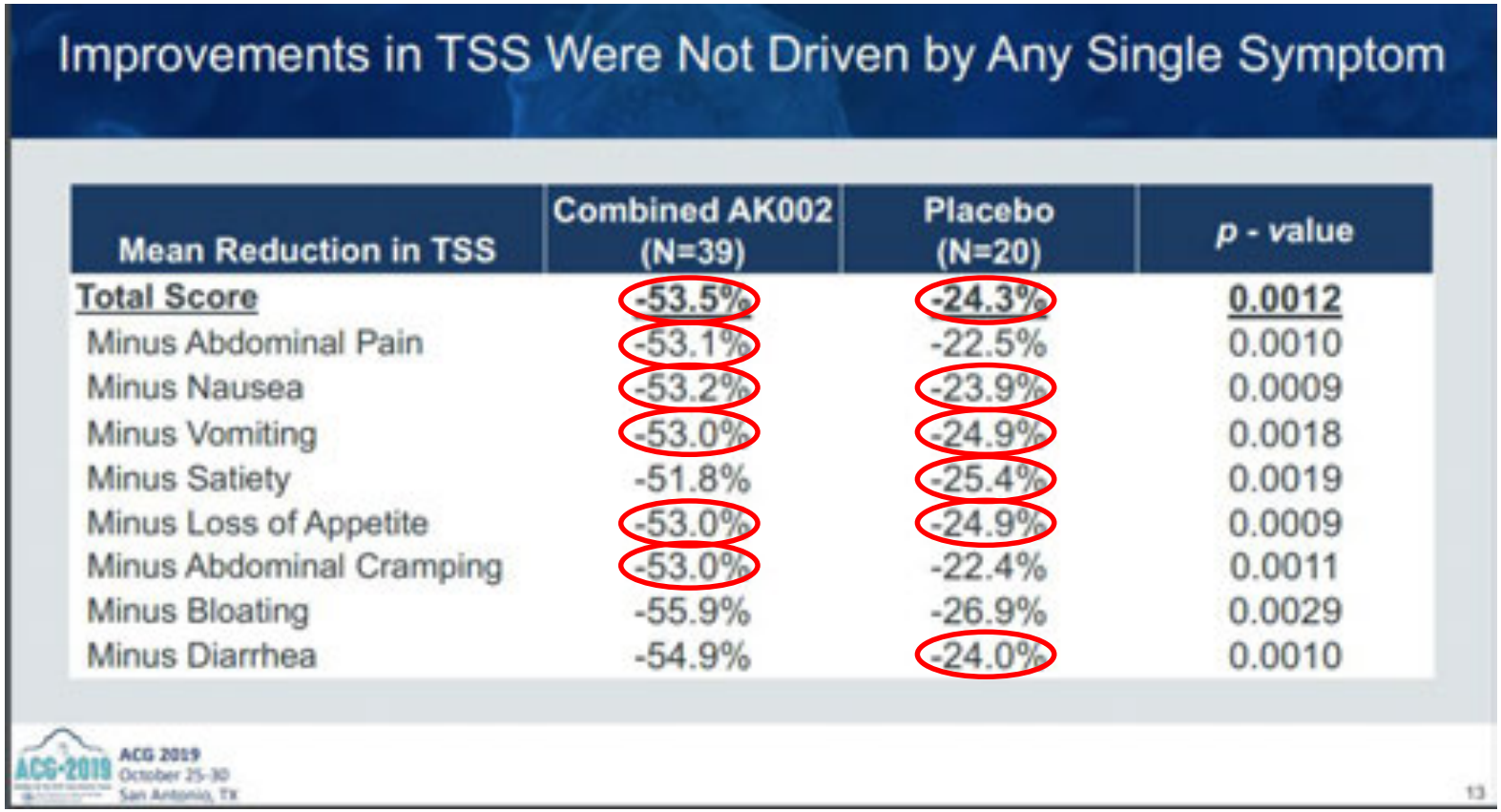
Primary and Secondary Endpoint p-values		AK002 Dose Groups High (n=20/16/21)	AK002 Dose Groups Low (n=19/12/22)	AK002 Dose Groups High/Low (n=39/28/43)	Placebo (n=20/13/22)
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	ITT	0.0260	0.1556	0.0359	-

Allakos

Source: CapitalIQ transcript; https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

Aside from Total Symptom Score over time, the UEG and ACG presentations showed improvement for each of the 8 symptoms measured in the PRO. Individual symptoms weren't disclosed over time, nor broken out by low and high dose. Irrespective, the unusual clustering in the data strains credibility. We question how the AK002 reductions magically cluster at 53%, and the placebo reductions at 24%. One would expect significant dispersion from subjective patient-reported scores and a small trial size, yet the data says it was virtually non-existent. The clinical literature clearly establishes the lack of symptom homogeneity in this population.



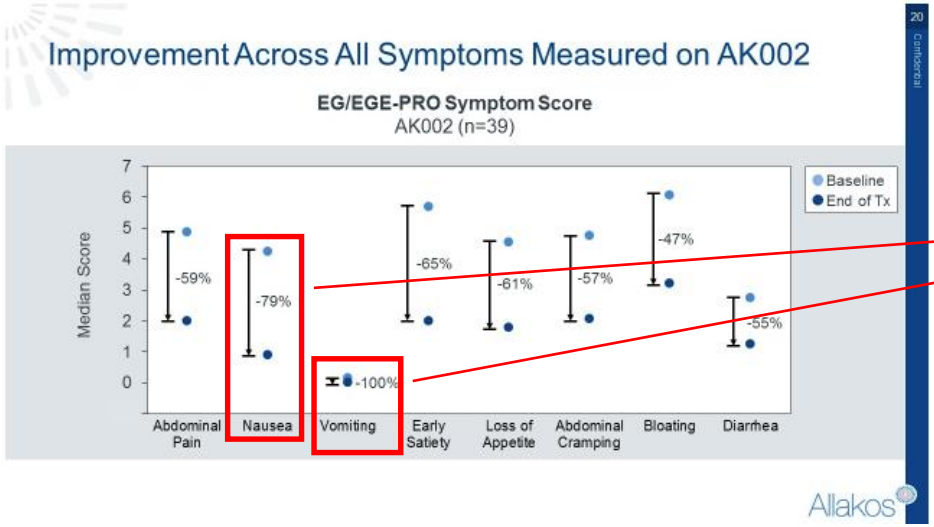
Improvements in TSS Were Not Driven by Any Single Symptom

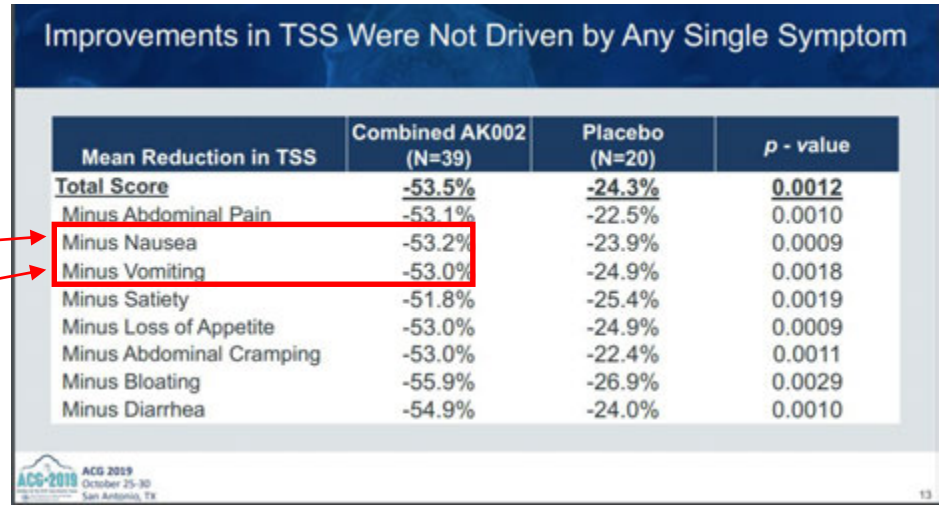
Mean Reduction in TSS	Combined AK002 (N=39)	Placebo (N=20)	*p* - value
Total Score	-53.5%	-24.3%	0.0012
Minus Abdominal Pain	-53.1%	-22.5%	0.0010
Minus Nausea	-53.2%	-23.9%	0.0009
Minus Vomiting	-53.0%	-24.9%	0.0018
Minus Satiety	-51.8%	-25.4%	0.0019
Minus Loss of Appetite	-53.0%	-24.9%	0.0009
Minus Abdominal Cramping	-53.0%	-22.4%	0.0011
Minus Bloating	-55.9%	-26.9%	0.0029
Minus Diarrhea	-54.9%	-24.0%	0.0010

Source: ACG presentation on ALLK IR site http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; red ours for emphasis.

Warning sign #11: Aside from shifting p-values, the incremental data shared since Aug 5th is troubling for other reasons

In addition to statistically suspect clustering, we note discrepancies between the new symptom-level data and that presented in the August 5th top-line results. The original read-out indicates virtually no vomiting at baseline or end of treatment, and hence a symptom reduction of "-100%". We have already noted how this claim is contradicted by Facebook posts by trial participants, not to mention incredulity by ENIGMA investigators. Nonetheless, the new slide indicates a 53.0% reduction in vomiting. Moreover, the original data claimed 79% reduction in nausea whereas the new slide states -53.2%. Similar discrepancies appear in early satiety, loss of appetite, and bloating.





Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; ACG presentation on ALLK IR site - http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f; red ours for emphasis.

Warning sign #12: Allakos' representation of only one drug-related serious adverse event in the ENIGMA trial conflicts with numerous Facebook posts by trial participants or their families. If a company misreports one critical piece of data, we wonder what else may be misreported: there is rarely just one cockroach. We are concerned that Allakos raised ~$400MM days after the ENIGMA results with disclosure that appears to be flatly contradicted by patients.

Allakos states there was only one drug-related serious adverse event and claims that it *"recovered within 24 hours with no further sequelae."*

During the topline results call, the Chief Medical Officer added, *"And we didn't find any other significant adverse event. So worthwhile to mention here that there don't seem to be any adverse event outside the infusion windows."*

This claim is in contrast to Facebook posts by participants in the trial, which indicate a number of severe adverse events by multiple patients. The prevalence of these posts suggests that adverse events may have occurred in other patients who weren't posting online.

One patient reported being admitted to the hospital three times, after which she was "pulled off the study." Allakos says the only reaction during the trial resolved within 24 hours, but the patient describes one hospital admission lasting a week, and that she was only discharged because her insurance wouldn't cover a longer stay. She listed other reaction symptoms as "severe" and "super severe."

Warning sign #12 (cont'd): Allakos' representation of only one drug-related serious adverse event in the ENIGMA trial conflicts with numerous Facebook posts by trial participants

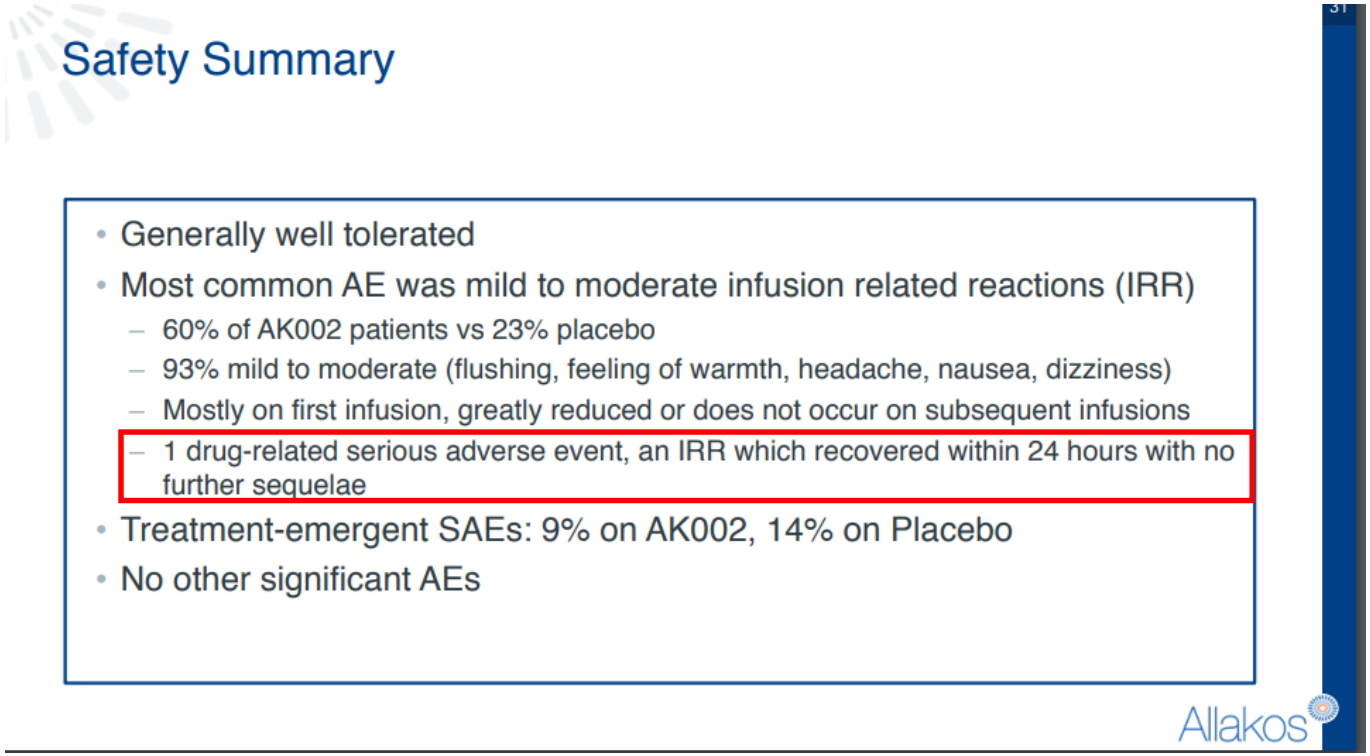
Another person described a "horrific reaction" following infusion, and visiting the emergency room following another reaction.

We additionally note accounts of severe migraines leading to episodes of blindness. Critically, the person states that the trial investigator was "very concerned" and "is reporting it as a possible adverse side effect." Given that at least one of these episodes led to an ER visit, we wonder why the side effect wouldn't be classified as "serious."

Warning sign #12: Allakos claims about adverse events are contradicted by online patient accounts

Allakos claimed only one drug-related serious adverse event and claims that it "recovered within 24 hours with no further sequelae."

"We had 1 drug-related serious adverse event, an infusion reaction which recovered within 24 hours with no sequelae. If you look at the total number of treatment-emergent serious adverse event, the incident was 9% on AK002 versus 14% on placebo. ***And we didn't find any other significant adverse event. So worthwhile to mention here that there don't seem to be any adverse event outside the infusion windows****." – Allakos Chief Medical Officer, Aug 5, 2019, EG/EGE study results call*

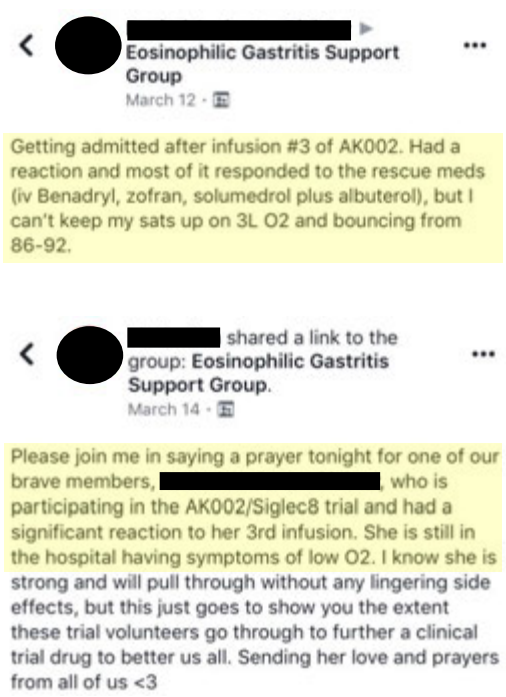


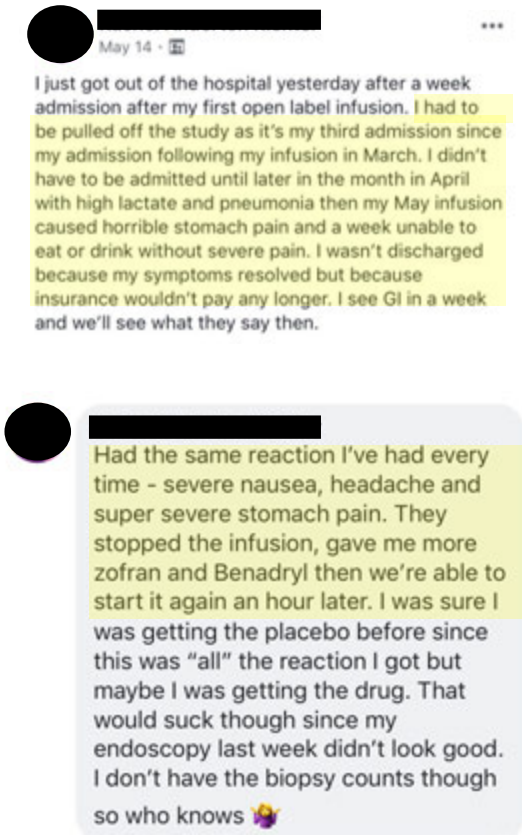
Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; CapitalIQ transcripts; red ours for emphasis.

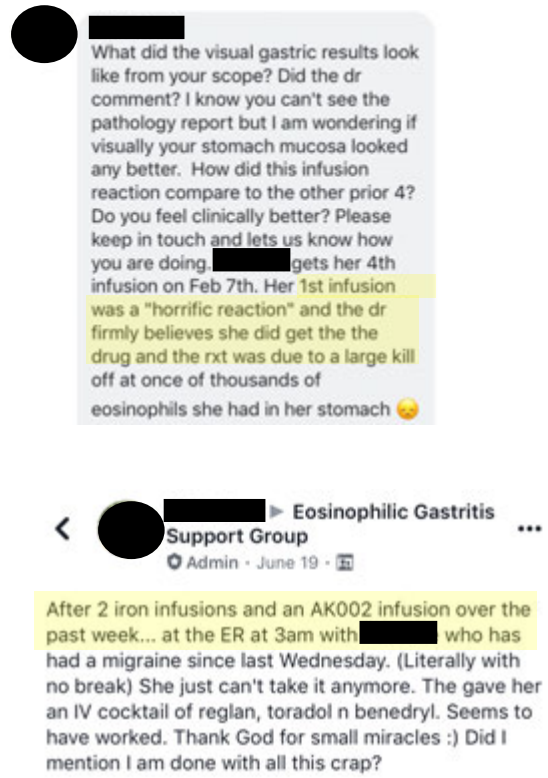
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #12: Allakos claims about adverse events are contradicted by online patient accounts

The claim of only one severe adverse event is in contrast to Facebook posts by participants in the trial, which indicate a number of severe adverse events by multiple patients. The prevalence of these posts suggests that adverse events may have occurred in other patients who weren't posting online. One patient reported being admitted to the hospital three times, after which she was "pulled off the study." Allakos says the only reaction during the trial resolved within 24 hours, but the patient describes one hospital admission lasting a week, and that she was only discharged because her insurance wouldn't cover a longer stay. She listed other reaction symptoms as "severe" and "super severe." Another person described a "horrific reaction" following infusion, and visiting the emergency room following another reaction.





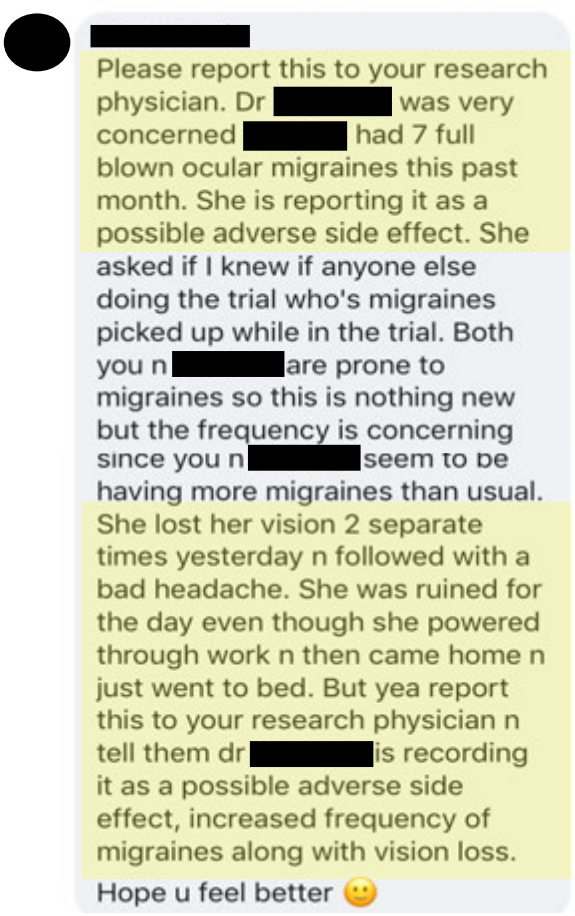


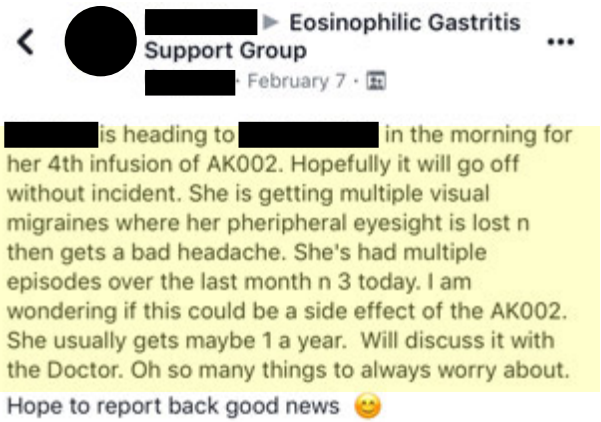
Source: https://www.facebook.com/groups/258285487951166/

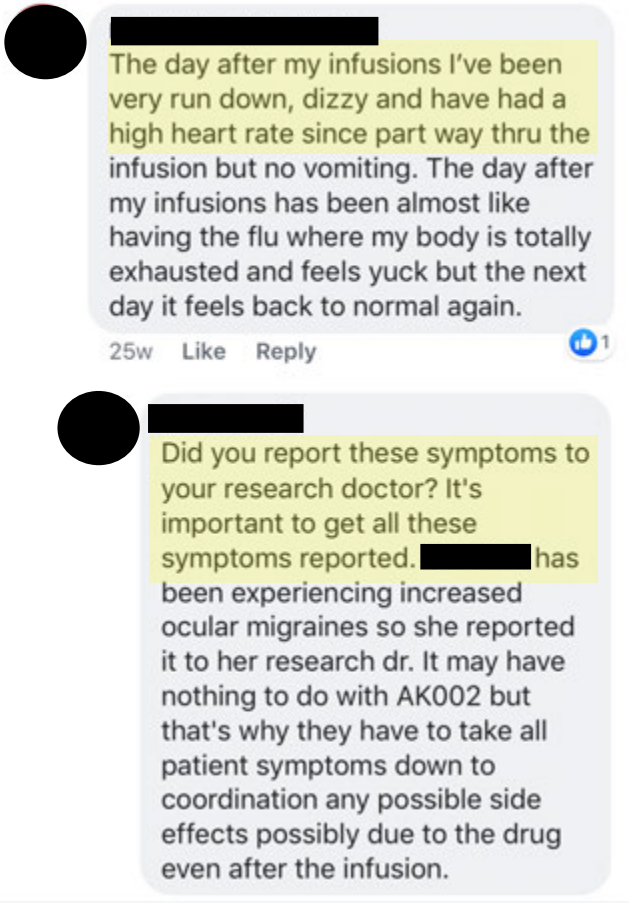
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #12: Allakos claims about adverse events are contradicted by online patient accounts

We note accounts of severe migraines leading to episodes of blindness. The post describes the typical frequency of one ocular migraine per year, versus as many as 3 in one day since being on the study. Critically, the person states that the trial investigator was "very concerned" and "is reporting it as a possible adverse side effect." Given that at least one of these episodes led to an ER visit, we wonder why the side effect wouldn't be classified as "serious."







Source: https://www.facebook.com/groups/258285487951166/

Warning sign #13: Allakos reported a lack of vomiting at baseline and end of treatment in the ENIGMA trial and omitted "vomiting" in the list of adverse events - representations which are wildly inconsistent with patient accounts on Facebook. Trial investigators were incredulous at Allakos' claim, raising worrying questions for investors given that vomiting is one of the most prevalent symptoms in the EGID patient population.

A trial investigator – a prominent physician in the EGID space – expressed incredulity, stating that vomiting is such a huge symptom within the patient population that the lack of vomiting in the Allakos data *"doesn't make any sense."*

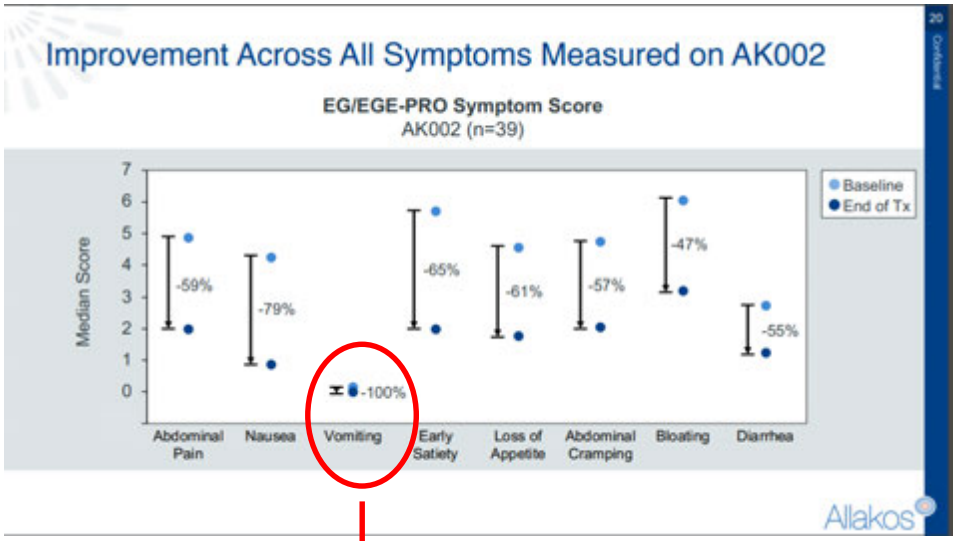
Even more troubling, Facebook posts by at least four trial participants or their families discuss vomiting in detail at 1) baseline, 2) during infusion, and 3) during the trial in settings other than infusion.

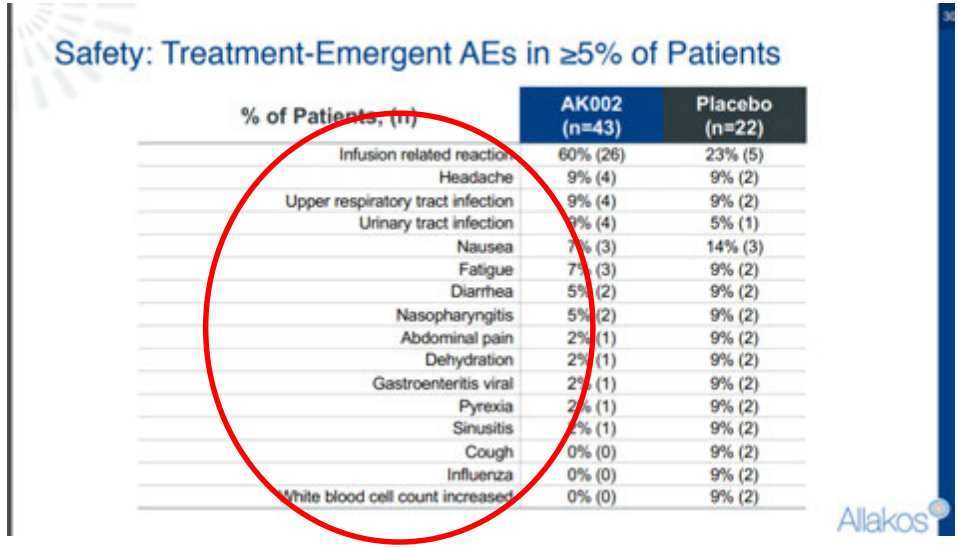
Given the magnitude of the discrepancy between Allakos' claims and those of patients, we wonder what other troubling discrepancies and surprises may await investors.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #13: Allakos claims about vomiting are inconsistent with online patient accounts

Allakos' symptoms slide reports a conspicuous lack of vomiting, at baseline or end of treatment. Moreover, "vomiting" isn't stated in the table of adverse events. The presentation states that safety was evaluated on the ITT population, meaning the safety data below includes all 65 patients in the trial.





Zero vomiting at baseline or during trial

The list of adverse events excludes mention of "vomiting."

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #13: Allakos claims about vomiting are inconsistent with online patient accounts

Allakos' claim of no vomiting raises worrying questions for investors. Vomiting is one of the most common symptoms within the patient population in the trial. One of Allakos trial investigators – a prominent key opinion leader in the EGID space – was incredulous and troubled at the company's assertions.

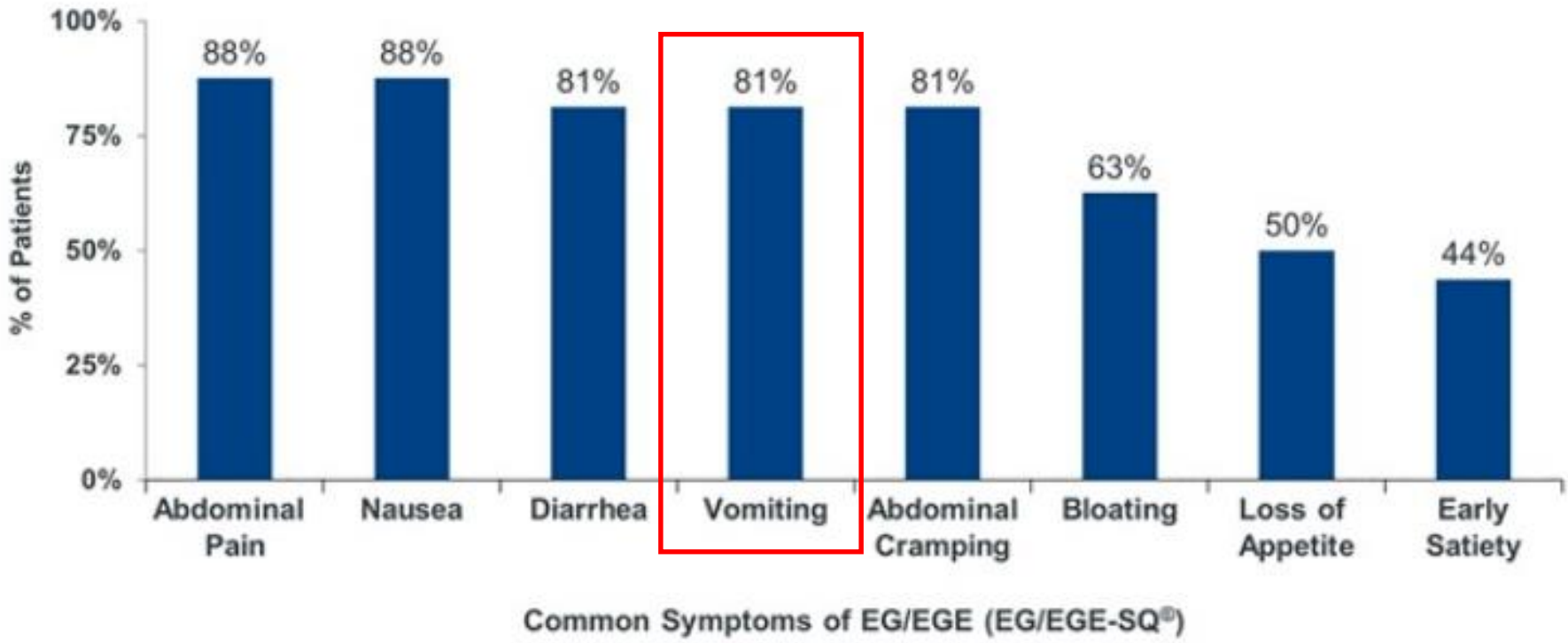
"Page 20 of their slide presentation says zero vomiting. ***Vomiting is a huge symptom. Most patients have vomiting. N=39 in the active arms and no vomiting. How did they find 39 patients without vomiting?*** *To me the biggest concern is the vomiting thing.* ***Maybe they made a mistake. It doesn't make any sense."*** *– Allakos ENIGMA trial investigator and a prominent physician in the EGID space.*

Source: Seligman expert consultation

Warning sign #13: Allakos claims about vomiting are inconsistent with online patient accounts

Allakos investigators published a poster at ACG in October 2019, on the development of the PRO instrument that ENIGMA patients used to journal their symptoms. Although the PRO was developed with a mere 16 patient interviews – we discuss flaws in the ENIGMA PRO in a later section – the investigators stated that 81% of EG/EGE patients exhibit vomiting.

"Development of a Patient Reported Outcome (PRO) Questionnaire to Assess the Symptoms of Eosinophilic Gastritis and Gastroenteritis (EG/EGE-SQ©)"



Source: https://journals.lww.com/ajg/Fulltext/2019/10001/Development_of_a_Patient_Reported_Outcome__PRO_.1247.aspx#pdf-link; red ours for emphasis.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #13: Allakos claims about vomiting are inconsistent with online patient accounts

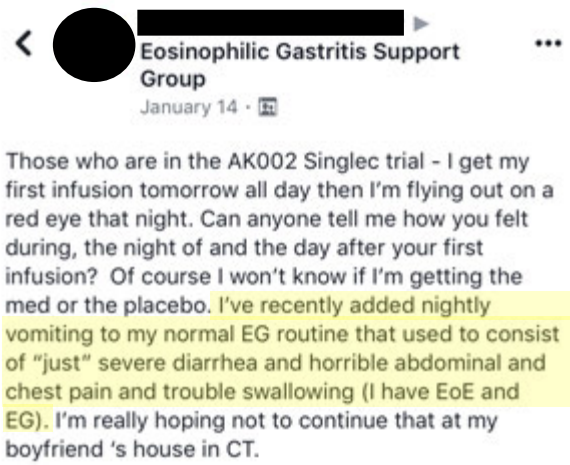
The trial doctor's concern about Allakos' truthfulness is supported by Facebook posts by at least four different patients or their families, which establish the prevalence of vomiting as a feature of the trial. Comments such as "since 2am I've been vomiting nonstop", or ones describing daily vomiting as a baseline symptom entered in the daily journal, followed by replies instructing participants to report the symptoms to study doctors, leave no ambiguity.

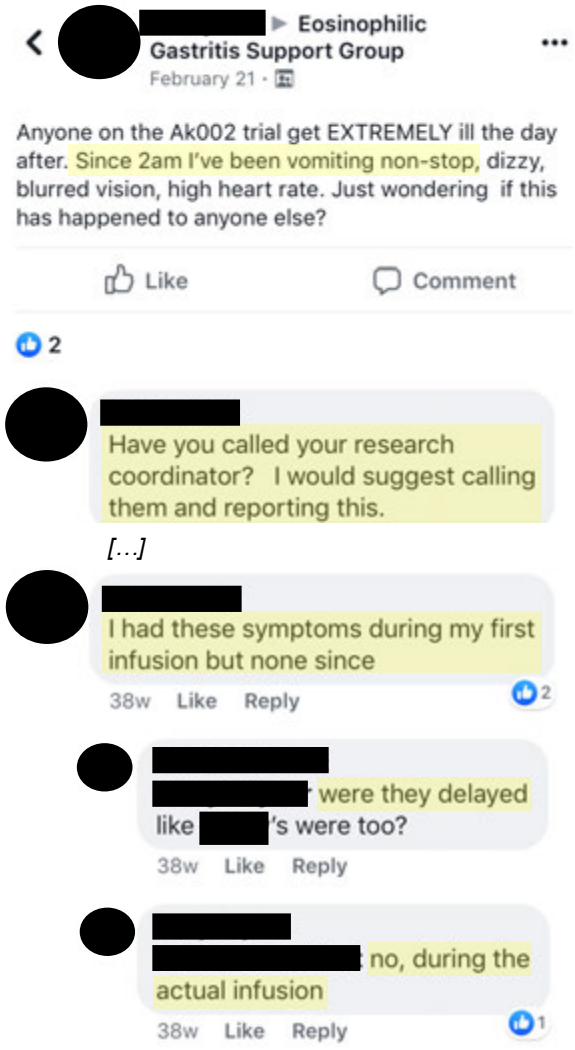
Source: https://www.facebook.com/groups/258285487951166/

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #13: Allakos claims about vomiting are inconsistent with online patient accounts

The number of posts by different patients referencing vomiting stands in troubling contrast to the company's representations to investors. Discussion chains clearly discuss vomiting during the trial and even during infusion, with replies further recommending "calling [the research coordinator] and reporting this." If patient posts contradict Allakos on one critical issue, we wonder what else could be misrepresented.





Source: https://www.facebook.com/groups/258285487951166/

Warning sign #14:* *Unclear and shifting trial timelines, in apparent violation of the pre-specified protocol, suggestive of cherry-picking timeframes to engineer favorable results*. *The pre-specified protocol was already concerning given that tissue eosinophil and PRO endpoints were to be measured at different intervals. Given the numerous red flags around Allakos' conduct and the trial's integrity, we find the lack of clarity worrisome – and wonder if cutting the data at the original interval would have led to trial failure.

The ENIGMA protocol on ClinicalTrials.gov indicates that the primary endpoint of tissue eosinophils was to be assessed at day 99 (14 weeks), with the secondary endpoint of PRO symptom scores to be assessed at day 141 (20 weeks). However, the Aug 5th top-line presentation stated that endpoints were measured 2 weeks after last dose, or roughly 14 to 15 weeks. We have seen no data from Allakos beyond this point.

Moreover, other omissions and discrepancies lead us to wonder whether the disclosure of the new 14 week measurement point is even accurate. The October 29th ACG presentation omitted 'Endpoints assessed two weeks after last dose" and failed to state when the endpoints were measured. We do not believe this is accidental, as p-values have also changed.

A footnote buried in a later slide in the ACG presentation states "biopsy occurred 6 weeks post last dose instead of 2 weeks per protocol". This suggests that the company's disclosure on August 5th was inaccurate. Moreover, by the slide represents 2 weeks as "per protocol" – which is not per the protocol specified on ClinicalTrials.gov.

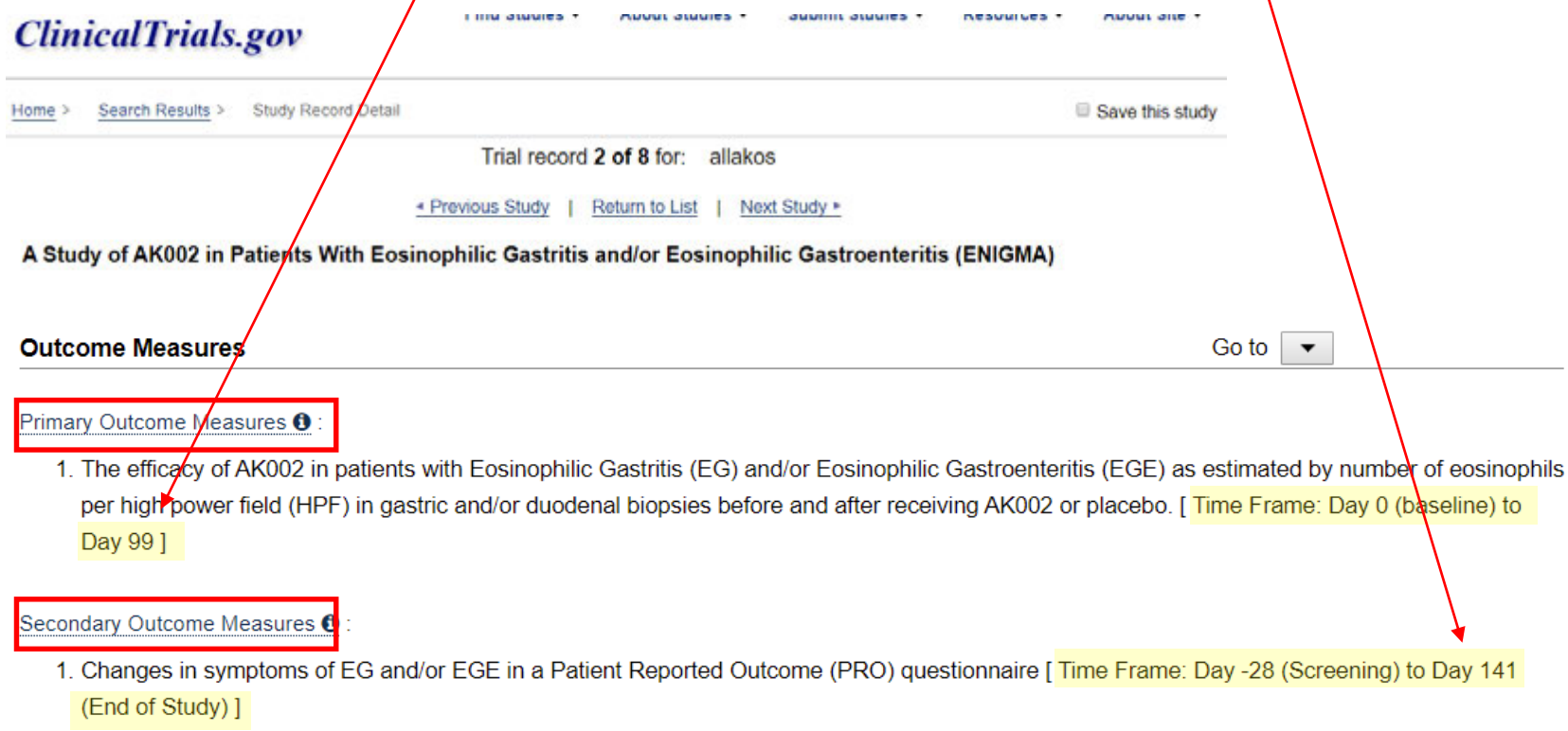
Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #14: Unclear and shifting trial timelines suggest cherry-picking to engineer favorable results

The pre-specified protocol in the ENIGMA trial stated a 28 day screening period, followed by a 141 day study period, for a total duration of 169 days (24 weeks). The primary endpoint of tissue eosinophils was to be assessed at day 99 (14 weeks), with the secondary endpoint of PRO symptom scores to be assessed at day 141 (20 weeks).

Tissue eosinophils/hpf to be measured at day 99/week 14

PRO symptoms to be measured at day 141/week 20



ClinicalTrials.gov

Home > Search Results > Study Record Detail

Save this study

Trial record **2 of 8** for: allakos

◂ Previous Study | Return to List | Next Study ▸

A Study of AK002 in Patients With Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis (ENIGMA)

Outcome Measures

Go to

Primary Outcome Measures :

1. The efficacy of AK002 in patients with Eosinophilic Gastritis (EG) and/or Eosinophilic Gastroenteritis (EGE) as estimated by number of eosinophils per high power field (HPF) in gastric and/or duodenal biopsies before and after receiving AK002 or placebo. [Time Frame: Day 0 (baseline) to Day 99]

Secondary Outcome Measures :

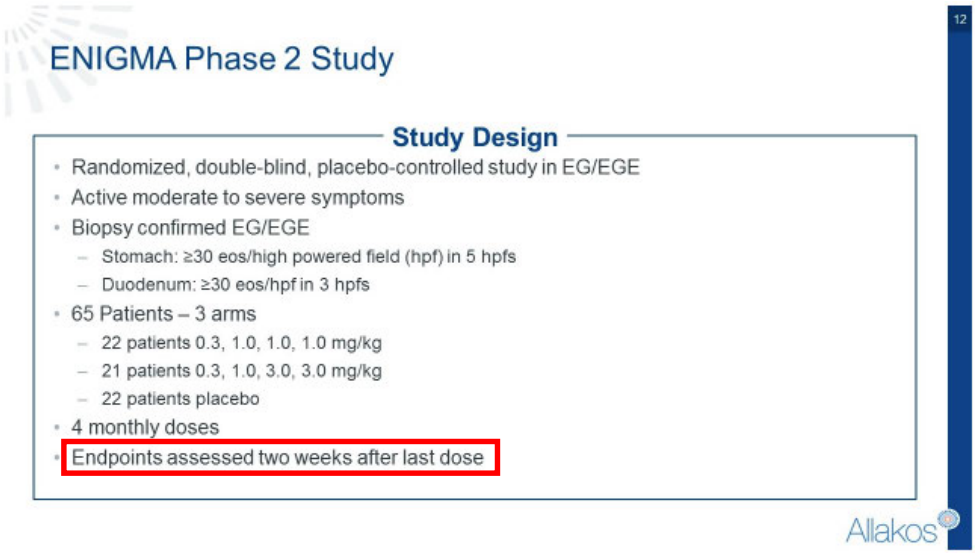
1. Changes in symptoms of EG and/or EGE in a Patient Reported Outcome (PRO) questionnaire [Time Frame: Day -28 (Screening) to Day 141 (End of Study)]

Source: https://clinicaltrials.gov/ct2/show/NCT03496571?term=allakos&draw=2&rank=2; red ours for emphasis.

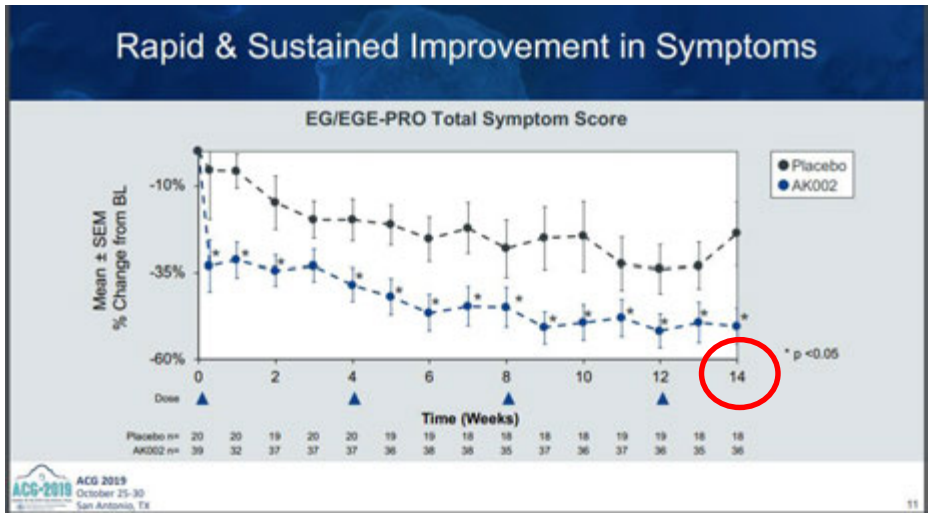
Warning sign #14: Unclear and shifting trial timelines suggest cherry-picking to engineer favorable results

However, the top-line presentation on Aug 5th stated that endpoints were measured 2 weeks after last dose, or roughly 15 weeks (four monthly doses at day 0, 30, 60, and 90 = 13 weeks plus 2 weeks). This suggests that tissue eosinophils were measured per protocol at 14 weeks (although we explain shortly why even this may not be accurate), but symptoms were not since the study specified measurement at week 20. The unexplained deviation from protocol is a red flag. Note that the company appears to have run the study itself and served as its "own CRO," We wonder if week 20 symptoms pointed to failure, leading the company to cherry-pick a shorter measurement period. We have seen no answer from Allakos for the protocol violation, nor any PRO symptom data after week 14.

August 5th results presentation states "Endpoints assessed two weeks after last dose."



ACG presentation on October 29 cuts off symptom data at week 14 – where is the missing data to week 20?

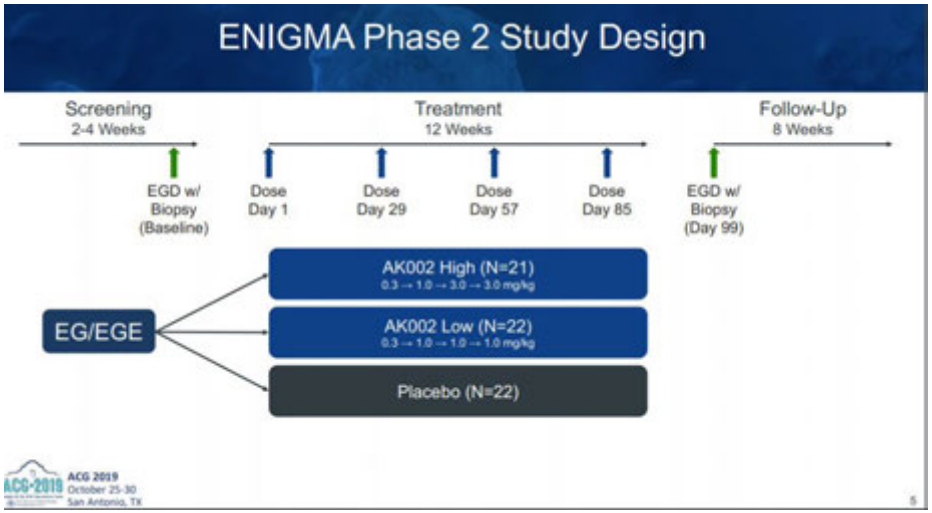


Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f ; red ours for emphasis.

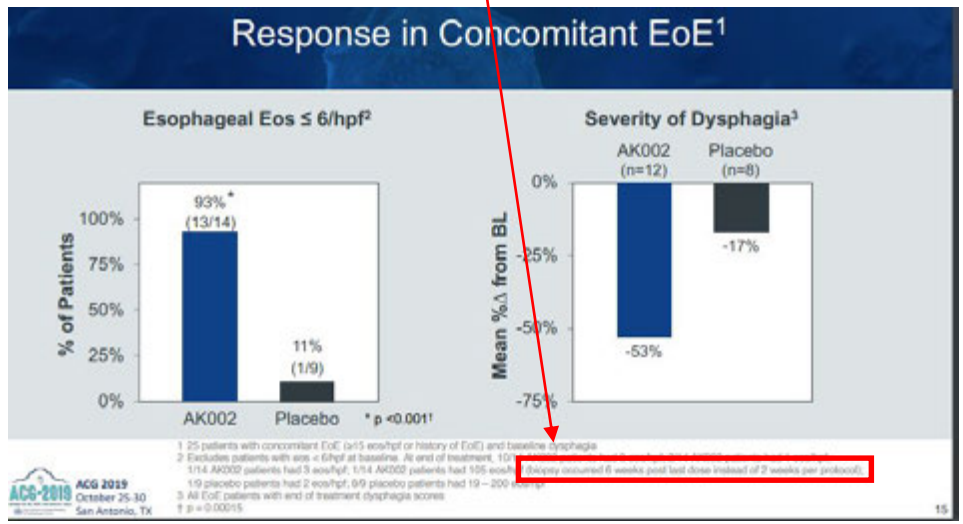
Warning sign #14: Unclear and shifting trial timelines suggest cherry-picking to engineer favorable results

Moreover, other omissions and discrepancies lead us to wonder whether even the new 14 week measurement endpoint is even accurate. The study design slide changed from August 5th to October 29th at ACG, omitting "Endpoints assessed two weeks after last dose" and failing to state when the primary and secondary endpoint were measured. We do not believe this is accidental, as the endpoints keep bouncing around. A footnote buried in a later slide in the ACG presentation states "biopsy occurred 6 weeks post last dose instead of 2 weeks per protocol". This suggests that the company's disclosure on August 5th was misleading. Moreover, the new slide appears misleading in its own right, as it states that "per protocol" was 2 weeks after last dose, which was not the protocol specified on ClinicalTrials.gov.

ACG study design slide on October 29 omits measurement periods for endpoints



ACG slide footnote #2 states "biopsy occurred 6 weeks post last dose instead of 2 weeks per protocol"



Source: http://investor.allakos.com/static-files/b9770b92-f110-4206-b7ad-64203997fb1f ; red ours for emphasis.

Warning sign #15: The ENIGMA trial used a fatally flawed PRO questionnaire whereby patients self-assessed their symptoms. Demonstrating symptom improvement is necessary per recent FDA guidance for EGID trials. The use of a reliable, validated PRO questionnaire is a pivotal determinant of how the FDA will evaluate Allakos' results, and Allakos' PRO was neither.

Eosinophil levels and symptoms are not correlated, raising the stakes for a PRO endpoint in phase 3. One Allakos EG/EGE trial investigator quantified the association between eosinophils and symptoms in a pediatric population, and concluded there was basically none (R^2 = .079).

The FDA's guidance document on PRO design specifically mentions their risks as a subjective and potentially faulty tool – further exemplified by a paper which lists at least five Allakos EG/EGE trial investigators as authors, which indicates that PRO's are unreliable in measuring EGID disease progress. The FDA's guidance document for EoE separately devotes an entire section on PRO's and asks companies to seek FDA input on a trial's PRO as early as possible.

Given the FDA's keen interest in the PRO used and their guidance to seek their input as early as possible, we note multiple red flags in Allakos "proprietary" "EG/EGE-SQ© Questionnaire.

Warning sign #15: The ENIGMA trial used a fatally flawed PRO instrument

The ENIGMA symptoms endpoint was assessed via a PRO (patient reported outcome) instrument, where patients self-reported how they felt over time on eight different measures such as nausea, cramping, and bloating. Demonstrating symptom improvement is necessary per FDA guidance, as other EGID trials have shown that even large eosinophil reductions do not necessarily translate into symptom reductions. The use of a reliable, validated PRO instrument is therefore a pivotal determinant of how the FDA will evaluate Allakos' results – based on FDA recent FDA guidance specifically for EGID's.

FDA guidance document for EoE trials

45 In patients with EoE, clinical features and histologic activity can vary independently. Patients
46 can have a reduction or resolution in signs and symptoms despite ongoing histologic activity;
47 conversely, patients can have histologic remission (defined as a change in peak eosinophils per
48 high power field (HPF) from a count greater than or equal to 15 to less than or equal to 6) with
49 persistent clinical symptoms (Dellon et al., 2013).

Source: https://www.fda.gov/media/120089/download; red ours for emphasis.

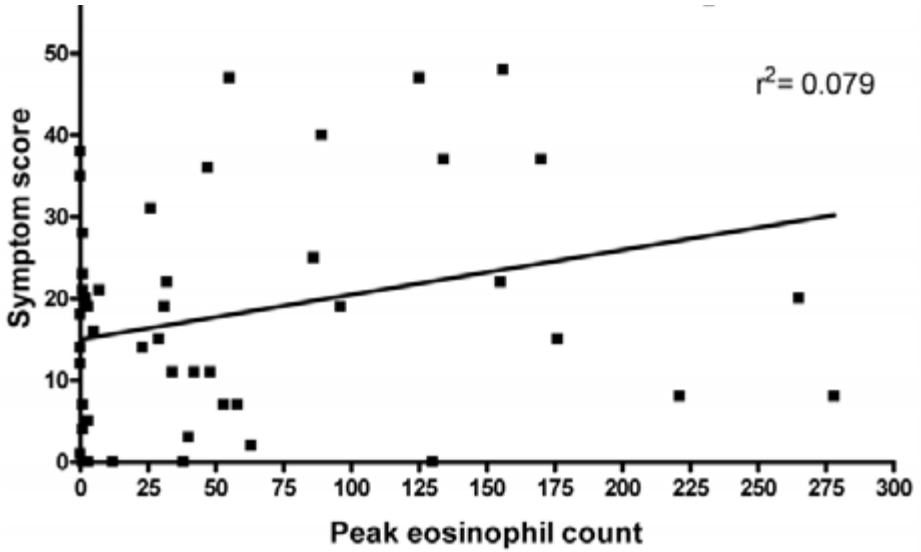
Warning sign #15: The ENIGMA trial used a fatally flawed PRO instrument

Eosinophil levels and symptoms are not correlated, and the disassociation is severe – raising the stakes for a PRO endpoint in phase 3. One Allakos EG/EGE trial investigator quantified the association between eosinophils and symptoms in a pediatric population, and concluded there was basically none (R^2 = .079). The degree of dispersion is remarkable and should be sobering for anyone excited about what the Allakos trial results – even if believed – actually prove. Patients with low eosinophils can have severe symptoms and vice versa. The dispersion is reinforced by competing trials.

Two papers by Allakos trial investigators on "marked disassociation" between histology and symptoms

Dissociation between symptoms and histological severity in pediatric eosinophilic esophagitis

Conclusions—Children with untreated EE had a higher PEESS than treated subjects. Symptoms persisted in 85% of EE patients despite histologic resolution and 10% with active EE reported no symptoms. Our data indicates a dissociation between symptoms and histology in pediatric EE.



Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2699182/pdf/nihms84699.pdf; red ours for emphasis.

clinical trials.[16] Although it is tempting to consider the use of histology as the primary determinant of therapeutic efficacy, a marked dissociation between symptoms and pathology is well recognized. This dissociation is likely explained by modification of eating behavior, subepithelial remodeling that is poorly assessed with standard biopsy technique, and a symptom-placebo response.

Source: https://www.jacionline.org/article/S0091-6749(18)30780-2/pdf

Warning sign #15: The ENIGMA trial used a fatally flawed PRO instrument

The FDA's guidance document on PRO design specifically mentions their risks as a subjective and potentially faulty tool. The FDA's guidance document for EoE separately devotes an entire section on PRO's and asks companies to seek FDA input on a trial's PRO as early as possible. The stakes in getting a PRO tool right are high – exemplified by a paper which lists at least five Allakos EG/EGE trial investigators as authors, which indicates that PRO's are unreliable in measuring EGID disease progress.

FDA guidance document for EoE trials

Sponsors developing drugs for the treatment of EoE should consider the following when using COA instruments, including PROs and ObsROs:

- FDA encourages sponsors to seek FDA input as early as possible and at important milestones throughout the drug development process to meet the challenges of COA development in this patient population.[7]

Source: https://www.fda.gov/media/120089/download

Paper by multiple Allakos trial doctors - *"Symptoms Have Modest Accuracy in Detecting Endoscopic and Histologic Remission in Adults With Eosinophilic Esophagitis"*

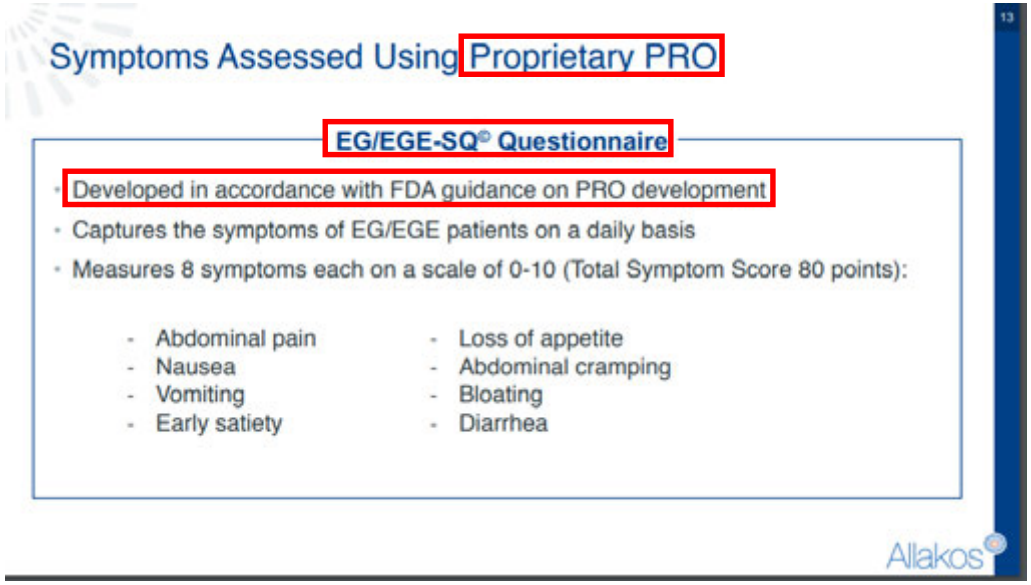
CONCLUSIONS—In patients with EoE, endoscopic or histologic remission can be identified with only modest accuracy based on symptoms alone. At any given time, physicians cannot rely on lack of symptoms to make assumptions about lack of biologic disease activity in adults with EoE. ClinicalTrials.gov, Number: NCT00939263.

In summary, given the imperfect concordance between patient-reported symptoms and endoscopic/histologic findings, physicians cannot rely on lack of symptoms to make assumptions about lack of biologic disease activity in adult EoE patients.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6011000/pdf/nihms799124.pdf; red ours for emphasis.

Warning sign #15: The ENIGMA trial used a fatally flawed PRO instrument

Given the FDA's keen interest in the PRO used and their guidance to seek their input as early as possible, we note multiple red flags in Allakos "proprietary" "EG/EGE-SQ© Questionnaire." Allakos EG/EGE results presentation suggests FDA validation, but the language states only that it was developed in accordance "with FDA guidance on PRO development" – which we infer as merely the generic guidance document. We can locate no validation or scrutiny for the company's PRO in the medical literature, and believe that Allakos' bespoke PRO will need to be replaced once the FDA weighs in, perhaps even inviting their as the FDA's EoE guidance document stresses the importance of first testing a PRO in phase 2.



FDA guidance on EoE endpoints emphasizes use of a "well-defined and reliable" PRO

Trials intended to support marketing approval of a drug for the treatment for EoE should evaluate a drug's effect on both signs/symptoms and the related underlying inflammation. Therefore, sponsors should assess coprimary endpoints in phase 3 trials as follows:

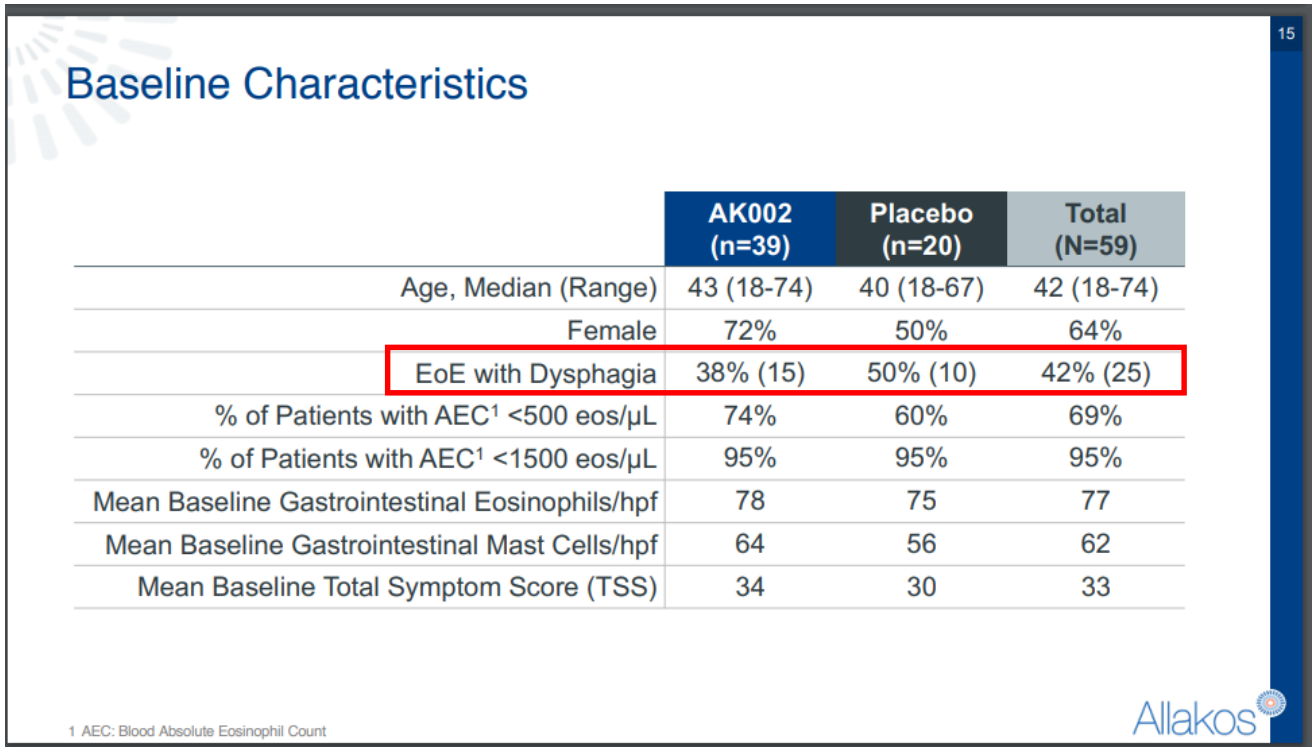
– Assess significant improvement from baseline in signs and symptoms, compared to placebo, using a well-defined and reliable COA instrument.

Source: https://www.fda.gov/media/120089/download

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #15: The ENIGMA trial used a fatally flawed PRO instrument

Other PRO's have been validated in the EGID space and discussed in the clinical literature by many of Allakos own EG/EGE trial investigators, making the decision to use a "proprietary" one worrisome. Shockingly, 42% of the ENIGMA trial population had EoE with dysphagia (difficulty swallowing), yet Allakos used a PRO which didn't even ask about dysphagia, a defining symptom of EoE. PRO's are valid for one disease type yet Allakos applied a crude questionnaire to a mixture of EG, EGE, EoE patients, rendering their phase 2 data dubious. In contrast, we note that a competitor's recent phase 3 trial in EoE[1] used the Dysphagia Symptom Score Questionnaire (DSQ), a validated instrument used for years[2]. We emphasize the stunning nature of a trial where the PRO isn't even tailored to the disease, as almost half of patients weren't asked about its characteristic symptom.



15

Baseline Characteristics

	AK002 (n=39)	Placebo (n=20)	Total (N=59)
Age, Median (Range)	43 (18-74)	40 (18-67)	42 (18-74)
Female	72%	50%	64%
EoE with Dysphagia	38% (15)	50% (10)	42% (25)
% of Patients with AEC[1] <500 eos/µL	74%	60%	69%
% of Patients with AEC[1] <1500 eos/µL	95%	95%	95%
Mean Baseline Gastrointestinal Eosinophils/hpf	78	75	77
Mean Baseline Gastrointestinal Mast Cells/hpf	64	56	62
Mean Baseline Total Symptom Score (TSS)	34	30	33

1 AEC: Blood Absolute Eosinophil Count

Allakos

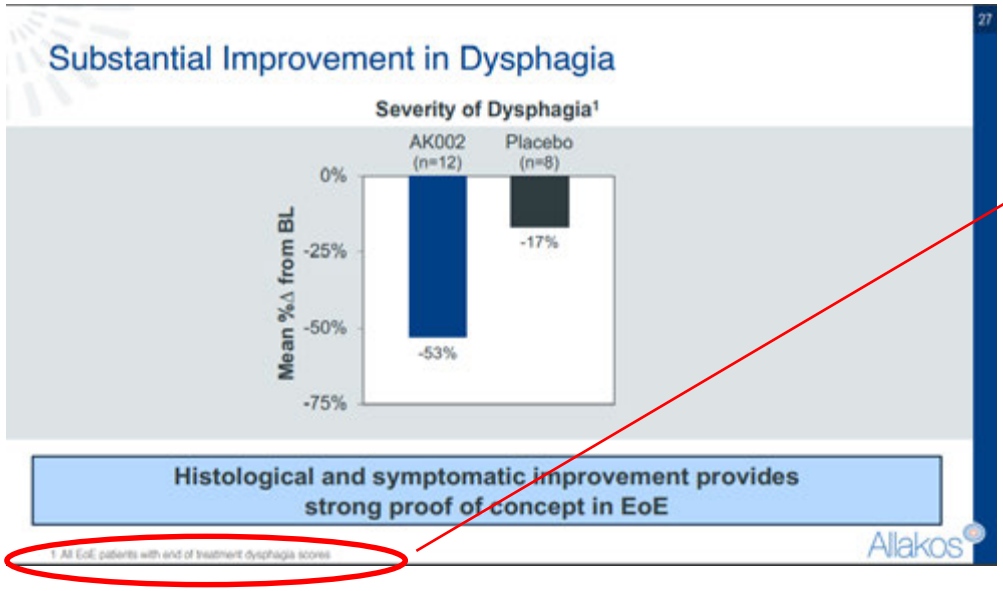
Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; [1]https://www.takeda.com/en-us/newsroom/news-releases/2019/first-ever-u.s.-pivotal-phase-3-clinical-study-in-eosinophilic-esophagitis-eoe-completes/; [2]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5934937/; red ours for emphasis.

Warning sign #15: The ENIGMA trial used a fatally flawed PRO instrument

Further illustrating the problems and discrepancies around the ENIGMA PRO, Allakos clearly states that their PRO measured only 8 symptoms – EXCLUDING dysphagia. Yet mysteriously, Allakos then proceeds to claim "substantial improvement in dysphagia" anyway. If the PRO didn't ask patients to score trouble swallowing, we wonder where this data is coming from, and whether Allakos is being straight with investors about its PRO and how data was actually collected.

Allakos' Chief Medical Officer comments on Aug 5th call

"Our PRO measures 8 symptoms on a scale from 0 to 10, 10 being the most severe. So the Total Symptom Score is 80 points. So a reduction in Symptom Score is a good thing. ***The 8 symptoms we looked at were: abdominal pain; nausea; vomiting, early satiety, which means fulfillment before ending a meal; the loss of appetite; abdominal cramping; bloating; and/or diarrhea."***



Footnote states "All EoE patients with end of treatment dysphagia scores"

PRO excluded dysphagia, so where are these "dysphagia scores" mysteriously coming from?

Is Allakos being truthful with investors about the composition of their PRO and what symptoms "we looked at"?

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm' CapitalIQ call transcript; red ours for emphasis.

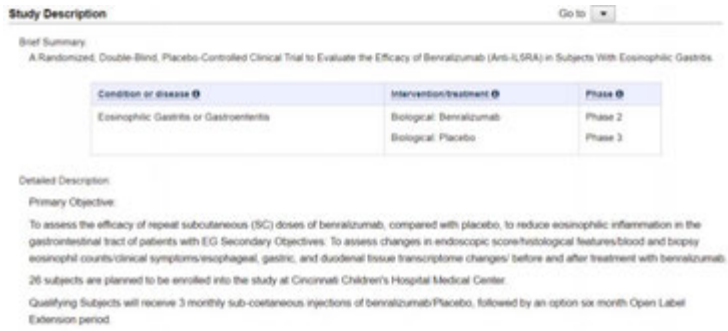
Warning sign #16: Significant trial design problems beyond a faulty PRO. The ENIGMA endpoints were superficial relative to competing EGID trials and FDA guidance, which incorporate a more robust battery of symptom, histologic, and endoscopic measures, even in phase 2. In particular, Allakos' failure to disclose endoscopy data – which trial investigators told us was collected – is worrisome. Papers by even ENIGMA investigators attest to the accuracy of endoscopic scoring.

Allakos' failure to disclose endoscopic information is an acute problem, given the availability of a validated, reliable visual scoring system. We note papers by multiple Allakos trial investigators, including Principal Investigator Evan Dellon, attesting to the accuracy of the EoE Endoscopic Reference Scoring System (EREFS), a "classification and grading system" for "major endoscopically identified, esophageal features of EoE (edema, rings, exudates, furrows, strictures)."

Warning sign #16: Significant trial design problems beyond a faulty PRO: superficial endpoints, no endoscopy data

Aside from a flawed PRO, we note other problems in the Allakos EG/EGE trial design and endpoints, which only consisted of tissue eosinophil reductions and patient-reported symptom scores. Competing EGID trials, taking their cue from the clinical literature and FDA guidance, utilize a far more robust set of endpoints across 1) symptomatic (using reliable, validated PRO's), 2) histologic (across multiple measures), and 3) endoscopic measures (using established scoring systems) – providing a roadmap for what we expect the FDA will require in phase 3. Allakos would have been reckless to not collect histologic data like blood eosinophil reduction as well on endoscopic features in the EG/EGE trial, and the company's silence on these measures points to problems in phase 3.

ClinicalTrials.gov entry for benralizumab trial for eosinophilic gastritis, currently underway



Study Description

Go to

Brief Summary:

A Randomized, Double-Blind, Placebo-Controlled Clinical Trial to Evaluate the Efficacy of Benralizumab (Anti-IL5RA) in Subjects With Eosinophilic Gastritis

Condition or disease	Intervention/treatment	Phase
Eosinophilic Gastritis or Gastroenteritis	Biological: Benralizumab	Phase 2
	Biological: Placebo	Phase 3

Detailed Description:

Primary Objective:

To assess the efficacy of repeat subcutaneous (SC) doses of benralizumab, compared with placebo, to reduce eosinophilic inflammation in the gastrointestinal tract of patients with EG Secondary Objectives: To assess changes in endoscopic score/histological features/blood and biopsy eosinophil counts/clinical symptoms/esophageal, gastric, and duodenal tissue transcriptome changes/ before and after treatment with benralizumab.

26 subjects are planned to be enrolled into the study at Cincinnati Children's Hospital Medical Center.

Qualifying Subjects will receive 3 monthly sub-cutaneous injections of benralizumab/Placebo, followed by an option six month Open Label Extension period.

Source: https://clinicaltrials.gov/ct2/show/NCT03473977

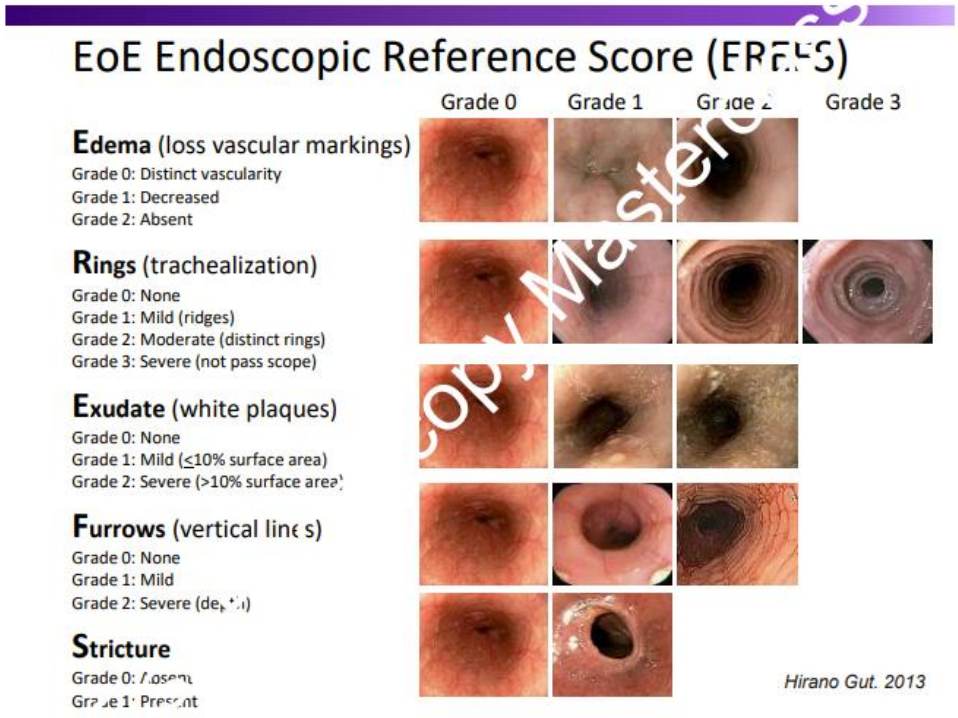
Note use of additional, more robust endpoints consistent with FDA EGID guidance

- **Changes in endoscopic features** before and after treatment as measured by standardized endoscopy scoring systems.
- **Changes in histologic features as measured by standardized histology forms** specific to the diseases of interest.
- **Changes in blood eosinophil counts**
- **Evaluate esophageal, gastric, and duodenal tissue transcriptome changes**; changes in expression of genes as assessed by whole genome RNA sequencing
- **Changes in quality of life** for pediatric EoE measured by the EoE-Quality of Life Scale A (range 0-96, with 96 being the most impaired)

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #16: Significant trial design problems beyond a faulty PRO: superficial endpoints, no endoscopy data

Allakos' failure to disclose endoscopic information is an acute problem, given the availability of a validated, reliable visual scoring system especially in EoE. We note papers by multiple Allakos trial investigators, including Principal Investigator Evan Dellon, attesting to the accuracy of the EoE Endoscopic Reference Scoring System (EREFS), a "classification and grading system" for "major endoscopically identified, esophageal features of EoE (edema, rings, exudates, furrows, strictures)." We spoke with an influential ENIGMA investigator, who bluntly opined that the "The FDA will use endoscopic findings more than eosinophil levels [in phase 3]. They are very objectively and quantitatively measurable, especially for EoE where there's a score and they're developing one for EG."



Source: https://www.e-eso.net/sessions/session_385007.do?methodcall=getSlides&idegrandround=682&download=0&Ticket=

Papers by principal investigator of the Allakos ENIGMA trial and a second study doctor

"The EREFS classification system identifies patients with EoE an AUC of 0.934; the score decreases with treatment, and histologic responders have significantly lower scores than non-responders. *This system can therefore be used to identify individuals with EoE and used as an endoscopic outcome measure to follow their response to treatment."*

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4690779/pdf/nihms725116.pdf

"[P]hysicians' global assessment of disease activity is largely based on endoscopic findings, rather than severity of histopathology. A recent study demonstrated that the EREFS score had a high degree of accuracy *for diagnosis of EoE and significant responsiveness to treatment."*

Source: https://www.cghjournal.org/article/S1542-3565(17)30313-0/pdf;

Source: Seligman expert consultations

Warning sign #17: The ENIGMA trial design lacks credibility and relevance for other reasons, which we expect to haunt the company in phase 3. The trial enrolled patients 18 and above, an odd choice given the prevalence of EG/EoE in patients <18 and recent FDA guidance on the importance of including adolescents in EGID trials. Trial investigators expressed incredulity at other aspects of the cohort selected, stating that it was atypical and marked by discrepancies. We get the sense that Allakos went out of its way to cherry-pick an unrepresentative population, and given that ALLK ran the study itself, we wonder if it was even randomized.

The ENIGMA trial enrolled patients 18 and above, while the benralizumab trial in EG enrolled younger patients starting at age 12 consistent with the FDA's recent comments to "encourage inclusion of adolescents (12-17 inclusive) in trials intended to provide substantial evidence of effectiveness to support regulatory approval." Both EG and EoE are prevalent in younger patients, and we question younger patients ability to withstand the severe infusion reactions we documented earlier.

Trial investigators expressed incredulity at other aspects of the patient population selected. The vast majority of real-world patients are on steroid therapy, yet Allakos suggests that only 35% of the active arm was on steroids.

An investigator pointed out that the patients in the trial were far less eosinophilic than those typically seen in the clinic. Similar selection discrepancies are visible in the EoE cohort. Allakos bizarrely suggests that the patient population exhibited no vomiting, troubling investigators who indicated that vomiting is a defining symptoms in EG/EoE patients.

Warning sign #17: Other trial design problems: unrepresentative trial population

The ENIGMA trial enrolled patients 18 and above, while the benralizumab trial in EG enrolled younger patients starting at age 12 consistent with the FDA's recent comments to "encourage inclusion of adolescents (12-17 inclusive) in trials intended to provide substantial evidence of effectiveness to support regulatory approval." Both EG and EoE are prevalent in younger patients, and we question younger patients ability to withstand the severe AK002 infusion reactions we documented earlier.

FDA guidance on "Pediatric Considerations" in EGID trials

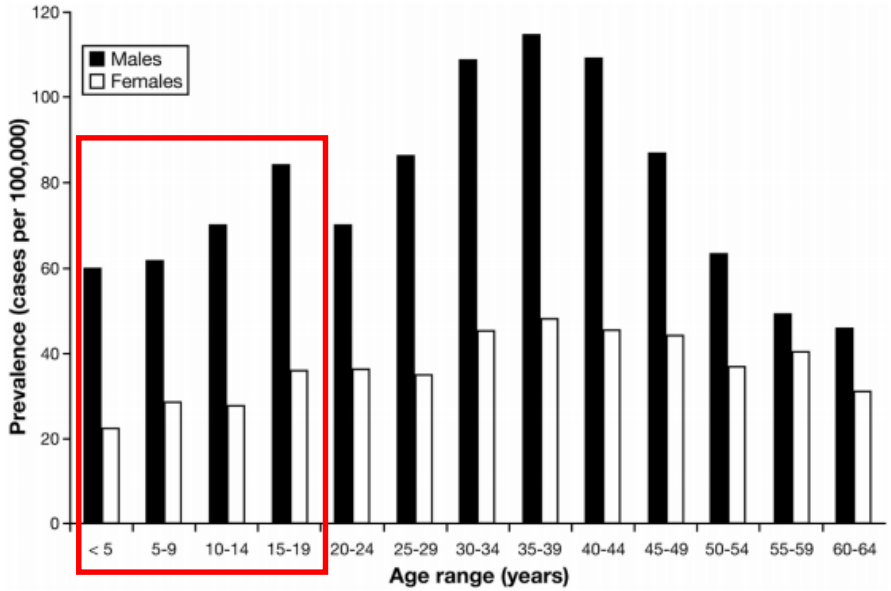
Sponsors developing drugs for the treatment of EoE should consider the following when enrolling pediatric patients in clinical studies:[10]

- We encourage the inclusion of adolescents (patients 12–17 years of age inclusive) in registration clinical trials, provided that preliminary safety and efficacy data in adult patients support enrollment. These trials should include design elements to ensure that all enrolled pediatric patients have the opportunity for exposure to active treatment (e.g., open-label extension, cross-over design) and should be followed by trials in patients younger than 12 years of age.
- We recommend including at least 40 adolescent patients per study arm in clinical studies that will include both adult and adolescent patients.
- For trials utilizing orally administered locally or topically acting corticosteroid drugs, growth measurements for pediatric patients should be standardized and replicated. Tanner stage should be obtained, and the growth data should be analyzed by pubertal stage (i.e., pre- and post-puberty).[11]

Source: FDA EOE guidance document https://www.fda.gov/media/120089/download;

*All red ours for emphasis

Distribution of EoE by age and gender



Source: https://www.cghjournal.org/article/S1542-3565(13)01304-9/pdf

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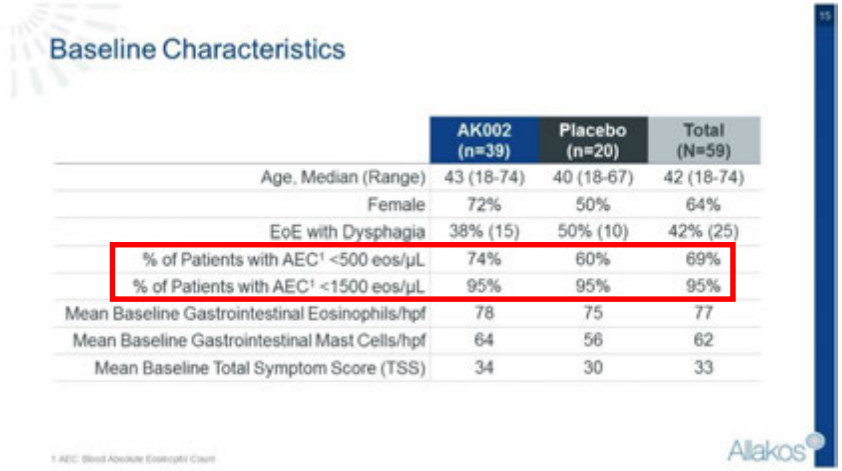
Warning sign #17: Other trial design problems: unrepresentative trial population

An ENIGMA trial investigator and a prominent physician/researcher in the space expressed incredulity at the trial's patient population and his concern that it was simply not representative. He indicated that the vast majority of EG/EoE patients are managed with steroids, yet steroid patients comprised only 35% of the ENIMGA cohort. He further indicated trial patients had baseline eosinophil levels which were too low to be reflective of the real world.

All Analyses Show Consistent Results

Primary and Secondary Endpoint	p-values	AK002 Dose Groups: High	Low	High/Low	Placebo
1° - Tissue Eosinophils % Δ from BL to Day 99	Per Protocol	<0.0001	<0.0001	<0.0001	-
	No Steroids	<0.0001	<0.0001	<0.0001	-
	ITT	<0.0001	<0.0001	<0.0001	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	Per Protocol	0.0009	0.0019	0.0008	-
	No Steroids	<0.0001	0.0001	<0.0001	-
	ITT	0.0008	0.0017	0.0007	-
2° - Total Symptom Score % Δ from BL to End of Study	Per Protocol	0.0012	0.0150	0.0012	-
	No Steroids	0.0016	0.0313	0.0027	-
	ITT	0.0260	0.1556	0.0359	-

Allakos



Baseline Characteristics

	AK002 (n=39)	Placebo (n=20)	Total (N=59)
Age, Median (Range)	43 (18-74)	40 (18-67)	42 (18-74)
Female	72%	50%	64%
EoE with Dysphagia	38% (15)	50% (10)	42% (25)
% of Patients with AEC[1] <500 eos/μL	74%	60%	69%
% of Patients with AEC[1] <1500 eos/μL	95%	95%	95%
Mean Baseline Gastrointestinal Eosinophils/hpf	78	75	77
Mean Baseline Gastrointestinal Mast Cells/hpf	64	56	62
Mean Baseline Total Symptom Score (TSS)	34	30	33

Allakos

Allakos slide indicates that only 35% of patients in active arm were on steroids (ITT subgroup n – no steroids n = 15, divided by n=43 for active arm)

"A lot of patients are steroid dependent. The symptoms flare if you take them off. ***Of the patients we see, more than 50% are on steroids, close to 80%.*** *That's how they're managed. It's rare to see a patient just managed by a diet. The papers from centers treating these patients show the majority are steroid dependent.* ***How do you get patients that are not on steroids in the study – the 60% of patients they say weren't on steroids?"*** ***– ENIMGA trial investigator/KOL***

Baseline eosinophil levels are low

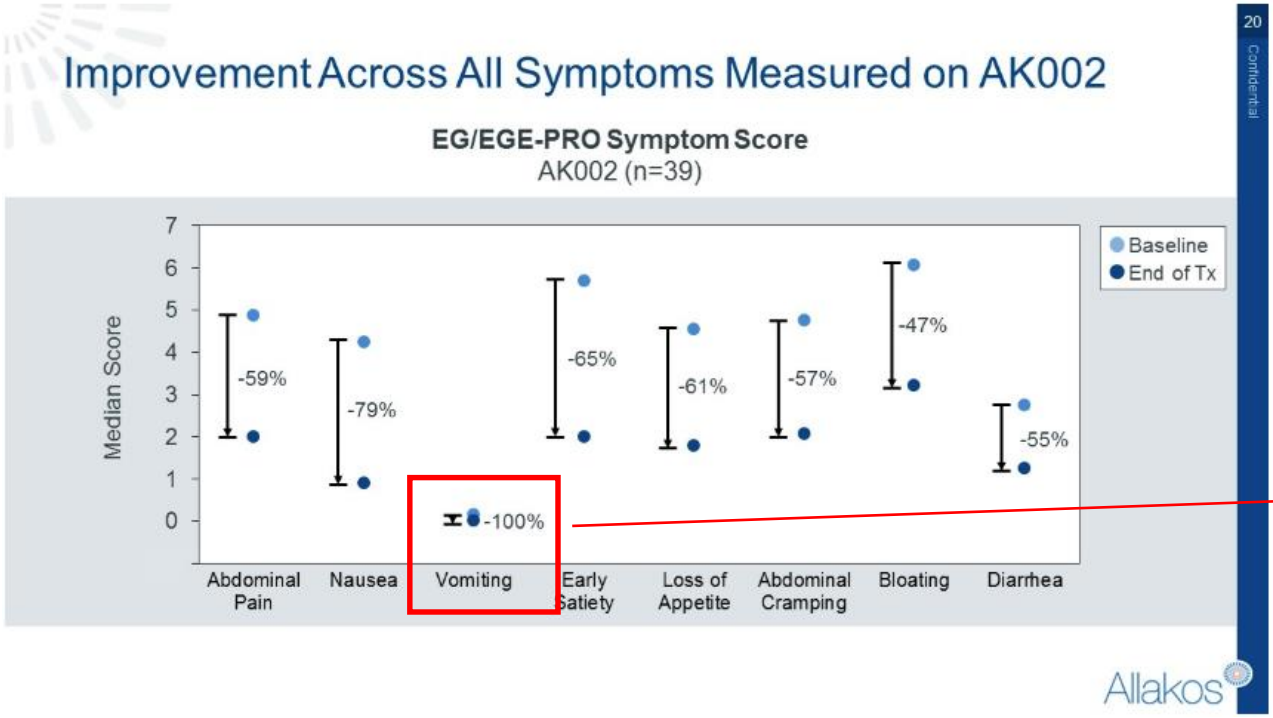
"These patients were not very eosinophilic. Page 15 of their presentation doesn't show a lot of eosinophils*. The blood eosinophils levels were 400. The average eosinophil levels in our patient population is around 1100. It's generally above 500. These may not be typical patients for whatever reason."* ***– ENIMGA trial investigator/KOL***

Source: Seligman expert consultations; https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #17: Other trial design problems: unrepresentative trial population

The investigator was further troubled by the purported lack of vomiting in the trial cohort. Vomiting is one of the defining symptoms of EG/EoE. We find it concerning that Allakos selected an unrepresentative study population, and given the company's role in running the study, we wonder what incentives may have precipitated these choices.

"Page 20 of their slide presentation says zero vomiting. ***Vomiting is a huge symptom. Most patients have vomiting. N=39 in the active arms and no vomiting. How did they find 39 patients without vomiting?*** *To me the biggest concern is the vomiting thing.* ***Maybe they made a mistake. It doesn't make any sense."*** *– Allakos ENIGMA trial investigator and a prominent physician in the EGID space.*



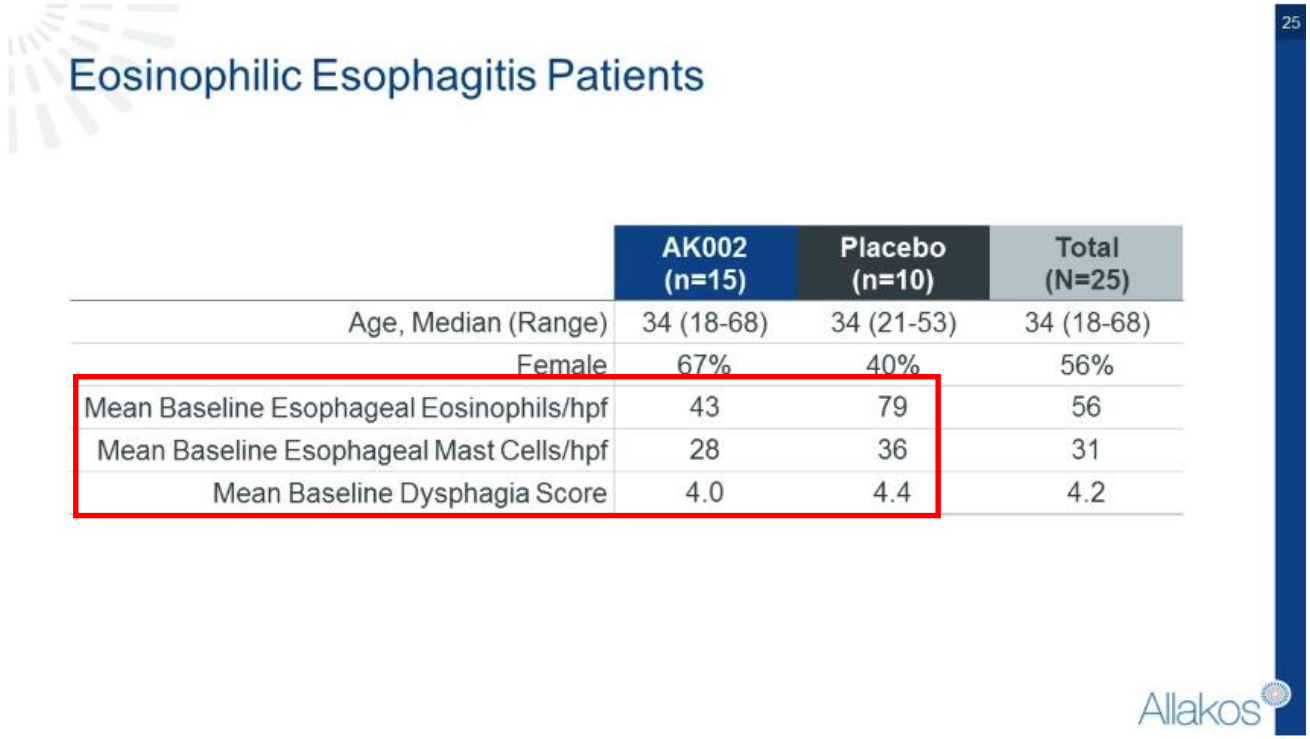
ENIGMA presentation indicates lack of vomiting

Source: Seligman expert consultations; https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #17: Other trial design problems: unrepresentative trial population

In addition, we note similar disparities in the EoE cohort, between the placebo and AK002 arms, with the placebo group exhibiting almost double the number of baseline eosinophils per hpf, as well as higher baseline mast cell counts and dysphagia scores. We fail to see how the trial conducted a valid comparison if one group is much sicker.

"As far as general methodology, one thing that is serious is the disparity in treatment and placebo subgroups*. On page 25, the baseline in placebo is way above the treatment group, and also elevated for mast cells, and their dysphagia score is higher.* ***The comparison here isn't fair. The placebo has more serious disease and symptoms."*** *– Professor of mathematics/biostatistics who we engaged to analyze Allakos' trial results*



Eosinophilic Esophagitis Patients

	AK002 (n=15)	Placebo (n=10)	Total (N=25)
Age, Median (Range)	34 (18-68)	34 (21-53)	34 (18-68)
Female	67%	40%	56%
Mean Baseline Esophageal Eosinophils/hpf	43	79	56
Mean Baseline Esophageal Mast Cells/hpf	28	36	31
Mean Baseline Dysphagia Score	4.0	4.4	4.2

Source: Seligman expert consultations; https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #18: The mystery of the missing blood eosinophil data. Allakos has touted AK002's powers in reducing blood eosinophils, but has withheld data ever since a phase 1 in healthy volunteers – remarkable silence given that subsequent AK002 trials have included it as an endpoint, not to mention it being a standard feature of competing trials. The ENIGMA trial disclosed baseline blood eosinophil levels, but shared ending ones only for tissue. Blood eosinophils are easily measured in CBC panels, while tissue biopsies are vulnerable to bias, irregular cell distribution, cherry-picking – and the pathologist's conflicts of interest. We detail uncomfortable questions lurking behind Allakos' strident assertions of AK002's inhibitory abilities.

Allakos has promoted AK002's ability to reduce blood eosinophil levels, starting with it phase 1 healthy volunteer study where it declared that the drug wiped out all eosinophils within one hour of administration.

After this phase 1, however, Allakos has gone silent. The withholding of blood eosinophil data in subsequent trials (mastocytosis, urticaria, allergic conjunctivitis, EG/EGE) is remarkable, despite the measure being a pre-specified endpoint in some of these studies, not to mention it being a standard feature of other studies in the space. The only data points we can locate since the phase 1 are tissue eosinophil reductions in the recent EG/EGE results - data we consider suspect as we believe it was collected by one pathologist with financial ties to Allakos.

Blood eosinophil levels are easy to measure and standard in CBC panels, and lack the problems of bias, irregular distributions, and cherry-picking that plague tissue counts via biopsy. Siglec-8 is highly expressed on blood eosinophils, making them the low hanging fruit for AK002,

Warning sign #18 (cont'd): The mystery of the missing blood eosinophil data.

assuming its mechanism of action is to be believed. Although Allakos continues to talk up AK002's anti-eosinophilic effects, the failure to share basic data to evaluate these claims is ominous.

Investors have taken AK002's eosinophil reduction abilities as a given, but beneath Allakos' strident assertions lies a simple reality: investors have only two crumbs in support of the Siglec-8 anti-eosinophil story – a one hour time interval for blood eosinophils in healthy volunteers, and claimed tissue reductions in the EG/EGE study.

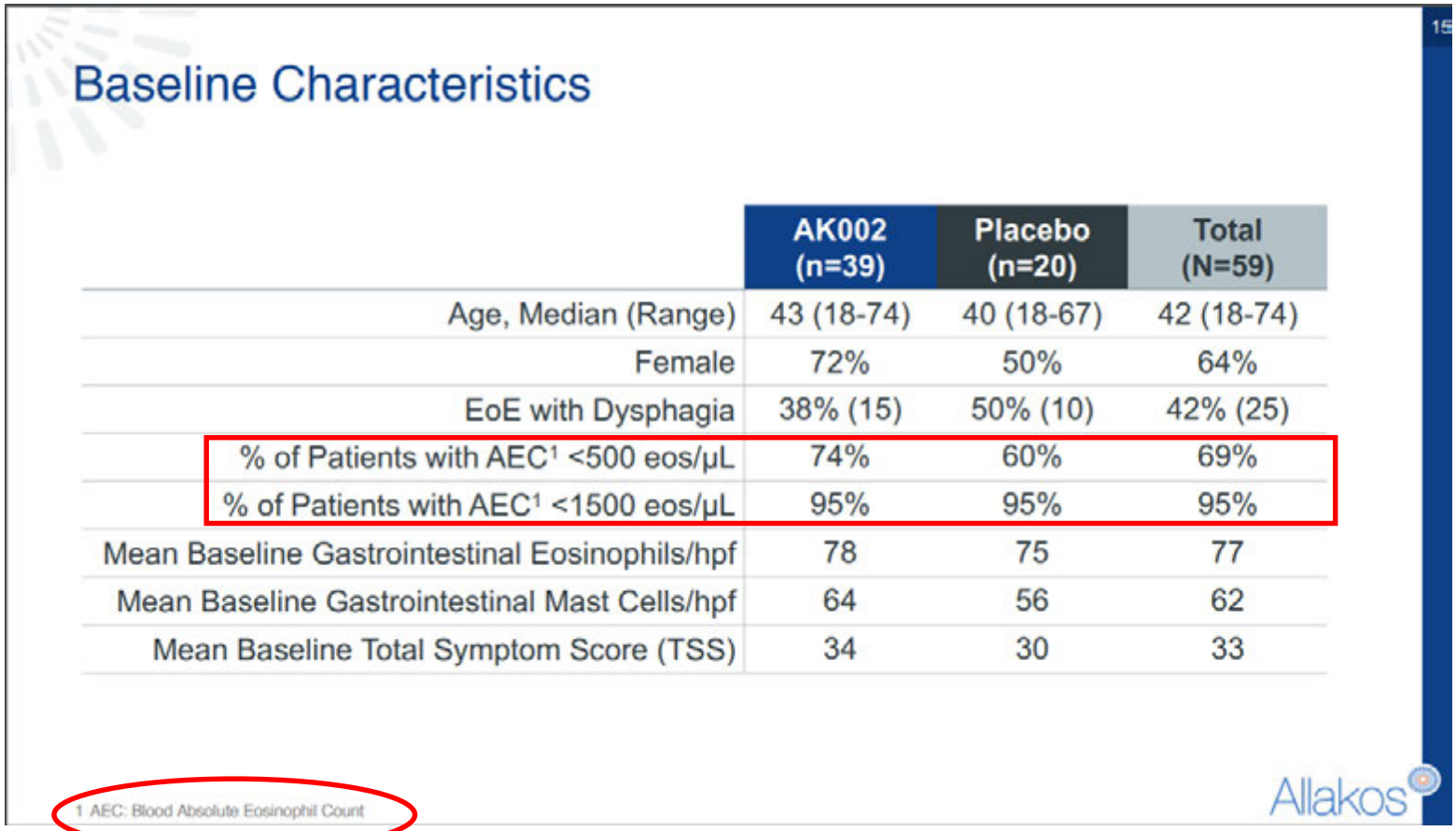
We can find no data from Allakos supporting AK002's ability to reduce blood eosinophil levels in symptomatic, eosinophilic patients, raising obvious questions:

1. If AK002 showed 100% reduction in blood eosinophils in healthy volunteers in the phase 1 in one hour, why has blood eosinophil data been withheld in subsequent trials, despite it being an endpoint and despite blood eosinophils being an easier target, given their level of Siglec-8 expression?

2. Given the company's claim that AK002 showed 93-97% reductions in tissue eosinophils in the EG/EGE trial, why was no data presented on blood eosinophil reductions, given that blood levels were shown at baseline? Did blood eosinophil levels also decline by 93-97%?

Warning sign #18: The mystery of the missing blood eosinophil data

Allakos' recent EG/EGE results provided baseline characteristics for blood eosinophil levels.



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1 AEC: Blood Absolute Eosinophil Count

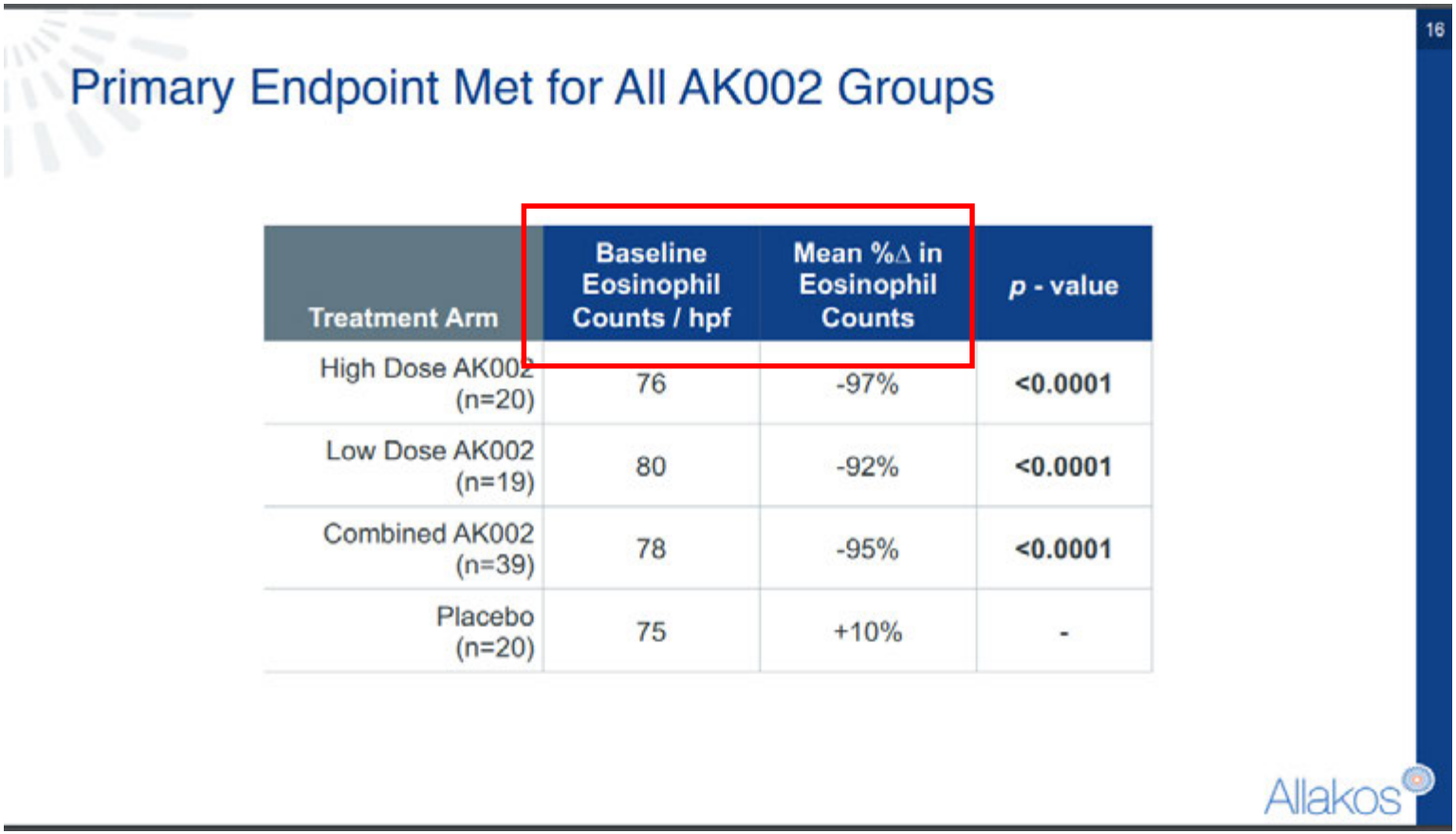
Allakos

"AEC: Blood Absolute Eosinophil Count"

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red emphasis ours.

Warning sign #18: The mystery of the missing blood eosinophil data

However, despite showing baseline blood eosinophil characteristics, Allakos then proceeds to withhold information on response rates, showing reductions for only tissue counts as measured by biopsy.



16

Primary Endpoint Met for All AK002 Groups

Treatment Arm	Baseline Eosinophil Counts / hpf	Mean %Δ in Eosinophil Counts	*p* - value
High Dose AK002 (n=20)	76	-97%	**<0.0001**
Low Dose AK002 (n=19)	80	-92%	**<0.0001**
Combined AK002 (n=39)	78	-95%	**<0.0001**
Placebo (n=20)	75	+10%	-

Allakos

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red emphasis ours.

Warning sign #18: The mystery of the missing blood eosinophil data

We find the omission striking given that Allakos' phase 1 touted AK002's ability to wipe out 100% of blood eosinophils within one hour of administration.

Clinical Results

AK002 was tested in a randomized, double-blind, placebo-controlled, dose-escalating Phase 1 trial conducted in Melbourne, Australia. 51 healthy volunteers were randomized to receive doses of AK002 (0.001, 0.003, 0.01, 0.03, 0.1, 0.3, or 1.0 mg/kg) or placebo. The primary endpoints of the trial were safety and tolerability. The secondary endpoints included pharmacokinetic and pharmacodynamic ("PK/PD") measurements, including changes in the absolute peripheral blood counts of eosinophils.

As shown in Figure 5, with respect to the secondary endpoints, all doses of AK002 tested resulted in complete depletion of blood eosinophils one hour after administration, clearly demonstrating the pharmacodynamic activity of AK002. The duration of depletion was dose-dependent with a single dose of 1.0 mg/kg of AK002 suppressing eosinophils for up to 84 days. AK002's pharmacokinetic half-life was determined to be 18 days.

Figure 5. Single Dose Placebo and AK002 Eosinophil Response

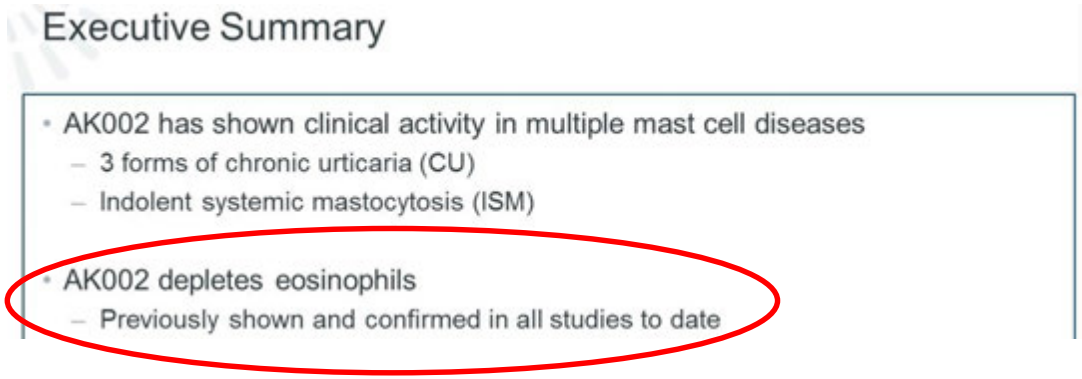
	Blood Eosinophils 10^3/mL				
Dose Cohort (mg/kg)	Placebo Pre-dose	Placebo 1 Hr Post-dose	AK002 Pre-dose	AK002 1 Hr Post-dose	Minimal Duration Eos Depletion
0.001	NA	NA	70	0	1 Day
0.003	120	70	160	0	2 Days
0.01	210	150	160	0	4-7 Days
0.03	150	150	160	0	7-14 Days
0.1	100	80	250	0	14-28 Days
0.3	180	140	180	0	28 Days
1.0	60	40	120	0	56-84 Days

Source: Allakos S-1 filing , https://www.sec.gov/Archives/edgar/data/1564824/000119312518219134/d447521ds1a.htm; red ours for emphasis.

Warning sign #18: The mystery of the missing blood eosinophil data

The claims of rapid, total eosinophil depletion from the phase 1 study are reinforced by Allakos' ongoing, emphatic comments about AK002's effect on blood eosinophils. The company states that "rapid depletion" has been shown in every one of their studies to date.

Allakos Investor Day presentation - Feb 19, 2019



Source: Allakos analyst day presentation https://www.sec.gov/Archives/edgar/data/1564824/000156459019003232/allk-ex991_199.htm; red ours for emphasis.

Results call for allergic conjunctivitis study – May 7, 2019

"We've recently put out a series of clinical data releases, including today's. ***The upshot is we've shown rapid depletion of blood eosinophils in all of those studies."*** *– Allakos CEO*

Analyst: "Just to clarify, are you seeing consistent reduction in peripheral eosinophils? And do the eosinophils stay suppressed *over the course of treatment? And just wondering if the eosinophils come back a little bit between infusions or do they stay suppressed?"*

Henrik Rasmussen, Allakos Chief Medical Officer: "Yes. So it's fair to say that we have seen consistent suppression of the eosinophils in all these indications, including the study we're talking about today. And we don't see any recurrence of the eosinophils…."

Source: CapitalIQ/Bloomberg transcripts

Warning sign #18: The mystery of the missing blood eosinophil data

Yet when given one opportunity after another to corroborate these assertions with data, the company has demurred. Blood eosinophil levels were shown at baseline in the EG/EGE study, but no response rate or P-value was provided – a continuation of the pattern seen in other trials. Blood eosinophils were even endpoints in the mastocytosis and allergic conjunctivitis studies, making the company's ongoing silence astounding and inexcusable.

The mastocytosis trial listed blood eosinophil counts and other histologic measures as endpoints, yet the trials results release on Feb 9, 2019 provided no data or even directional information on eosinophil (nor mast cell) reduction.

2. Evaluate the change from baseline in absolute peripheral counts of eosinophils and basophils. [Time Frame: Through out the study from screening to Day 85 or early term visit]
3. Evaluate the change from baseline in serum tryptase and eosinophil grande protein levels. [Time Frame: Through out the study from screening to Day 29 or early term visit]

Source: ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT02808793?term=allakos&rank=7; red ours for emphasis.

Blood eosinophil counts were also an endpoint in the allergic conjunctivitis study, yet the results press release was similarly radio silent.

Secondary Outcome Measures :

1. To evaluate the pharmacodynamics of AK002 in patients with AKC, VKC, or PAC as measured by changes from baseline in absolute peripheral blood counts of eosinophils and basophils [Time Frame: Starting pre-dose on day -1 to day 309 or early term visit]

Source: ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT03379311; red ours for emphasis.

Warning sign #18: The mystery of the missing blood eosinophil data

This raises a critical question for investors enamored of the ~95% eosinophil reduction in tissue biopsies in the EG/EEG study: were these reductions corroborated by blood eosinophil reductions? We note a recent letter to a medical journal, by an investigator from the Allakos EG/EGE trial and his colleagues, which indicated that blood eosinophils as well as their precursor cells are correlated with tissue eosinophil counts. Allakos' reluctance to share blood eosinophil data causes us to question the veracity of the tissue reductions in the EG/EGE trial, and therefore the entire theory behind AK002.

Eosinophil progenitor levels correlate with tissue pathology in pediatric eosinophilic esophagitis

Peripheral blood absolute eosinophil counts (AECs) positively correlate with tissue eosinophilia in patients with EoE.[9] Consequently, we compared blood EoP and AEC levels to EoEHSS scores in a subset of patients who had a documented AEC at the time of biopsy (n = 10; inactive = 4, active = 6; Fig 2). The peripheral blood EoP levels were significantly increased in patients with active disease and correlated with the EoEHSS composite ratio (Fig 2, *A* and *B*, respectively). In contrast, although there was a trend toward increased AECs in patients with active

Source: https://www.jacionline.org/article/S0091-6749(18)31576-8/pdf; red ours for emphasis.

Warning sign #18: The mystery of the missing blood eosinophil data

We note a 2017 paper in a medical journal which makes the same point in more detail, indicating high correlations between blood ('AEC") and tissue eosinophils in both adult and pediatric patients with EoE at baseline and after treatment. The paper states that "AEC predicted post-treatment eosinophilia…." For the avoidance of doubt, we further cite another study below reinforcing the linkage between blood eosinophils and eosinophil density in tissue. Although we are unable to locate papers which discuss correlations strictly for EG/EGE, the number of papers in similar EGID indications render the exercise superfluous.

Longitudinal Evaluation of Noninvasive Biomarkers for Eosinophilic Esophagitis

Multiple studies have investigated AEC levels in subjects with EoE. A small case series following 7 pediatric patients with EoE demonstrated elevated peripheral eosinophilia that correlated with disease activity.[9] Schlag et al[4] showed that AEC levels significantly correlated with esophageal eosinophil density in 51 EoE subjects, both at baseline and after treatment with budesonide. Although our study included both adults and children, it is interesting to note that both studies determined that AEC stood out among the multiple biomarkers that were being evaluated. Two other prospective studies also suggested levels of AEC

Conclusions: AEC, ECP, and EDN were higher in EoE subjects compared with controls and correlated with degree of esophageal eosinophilia. Furthermore, AEC predicted post-treatment eosinophilia, suggesting a potential role in monitoring EoE disease activity.

Source: https://www.ncbi.nlm.nih.gov/pubmed/27479142

**All red ours for emphasis*

Peripheral blood eosinophils and other non-invasive biomarkers can monitor treatment response in eosinophilic oesophagitis

Discussion

This prospective longitudinal placebo-controlled study demonstrates that treatment-induced changes of the activity of EoE is mirrored by non-invasive blood and serum biomarkers such as number of eosinophils in the peripheral blood as well as serum levels of ECP, CCL-26, CCL-17 and MCT. All these biomarkers decreased significantly in patients, who were successful treated with budesonide, but not in placebo recipients. However, only the levels of eosinophils

Source: https://onlinelibrary.wiley.com/doi/pdf/10.1111/apt.13386

Warning sign #18: The mystery of the missing blood eosinophil data

Also damning for Allakos, detailed phase 2 results for benralizumab – a competing drug we cover in detail in a later section, which is far ahead and which we believe renders AK002 irrelevant – were recently published in the New England Journal of Medicine and demonstrate tissue plus blood eosinophil reductions in addition to clinical improvement. The study focused on hypereosinophilic syndrome and hit the primary endpoint of blood eosinophil reduction, but also provided data for a subgroup with eosinophilic gastritis, showing superior reduction of gastrointestinal tissue eosinophils than AK002. We encourage investors to read the article and 54-page supplemental data package, as the contrast highlights the omissions and cherry-picking that characterizes Allakos behavior.

Benralizumab for PDGFRA-Negative Hypereosinophilic Syndrome

Eosinophils were ***"undetectable in the blood, bone marrow, and tissues after 12 weeks of benralizumab therapy."***

"Tissue samples obtained at week 24 showed ***nearly complete depletion of eosinophils (≤1 eosinophil per high-power field)*** *in a total of 52 gastrointestinal biopsy samples obtained from the seven patients with gastrointestinal eosinophilia…."*

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa1812185; supplemental data package: https://www.nejm.org/doi/suppl/10.1056/NEJMoa1812185/suppl_file/nejmoa1812185_appendix.pdf

Warning sign #19: The mystery of the missing mast cell data. The Allakos story hinges on AK002's ability to remove both eosinophils and mast cells, as both express Siglec-8. Either Siglec-8 inhibition works or it doesn't. Company materials suggest that mast cells are the driver of eosinophil "activation and recruitment." Yet given the centrality of mast cells to the story, the company's reluctance to share basic data mirrors the lack of disclosure on blood eosinophils. The scraps of data shared are troubling, and notably omit tryptase levels – the only relevant measure of mast cell activity. One of the world's top mast cell research scientists dismissed the Aug 5th ENIGMA mast cell claims as "not significant, relevant, or clinical effects."

Siglec-8 receptors are found on the surfaces of both eosinophils and mast cells. Allakos' CEO has described both cells as partners in the "inflammatory cascade," creating a major problem if AK002 fails to inhibit mast cells. Inhibiting only one cell type would cast doubt on the entire Siglec-8 premise.

Yet given the importance of mast cells to the Allakos story, the company's failure to share meaningful data on AK002's inhibitory effects is similar to its reticence on blood eosinophil counts. The first time we see meaningful mast cell data is in the August 5th ENIMGA results, and it explains Allakos' reluctance: AK002 failed to show statistical significance in mast cell reductions in two of three biopsy measures, and the data raises other troubling questions.

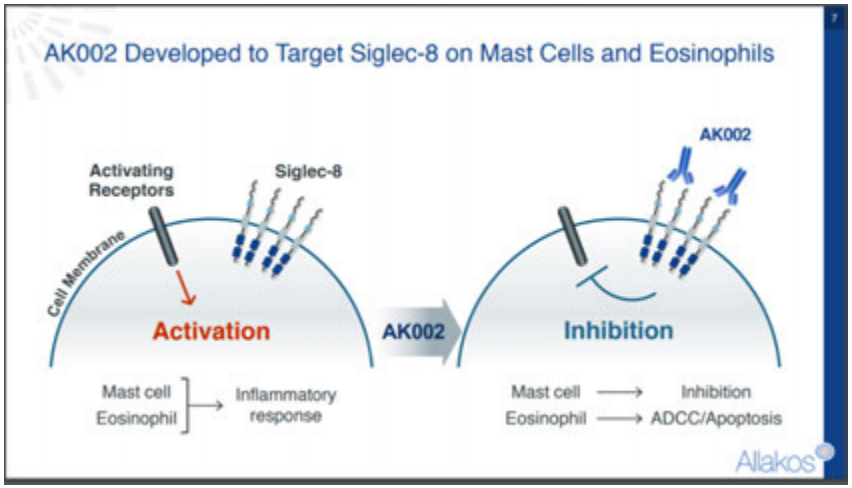
We believe that Allakos is sitting on other data beyond the ENIGMA trial which demonstrates that AK002 is a flop in reducing mast cells. Irrespective, the mast cell counts shown in the ENIGMA results are meaningless.

Warning sign #19: The mystery of the missing mast cell data (cont'd)

The only relevant and industry-standard measure of mast cell activity and inhibition is tryptase levels, measured by a simple blood test. We find Allakos' redirection to mast cell counts vs. activity to be a tactic that would never fly with peer-review or the FDA – leading one of the most prominent mast cell researchers in the world to dismiss the Aug 5th ENIGMA mast cell claims as *"not significant, relevant, or clinical effects."*

Warning sign #19: The mystery of the missing mast cell data

The Allakos story hinges on AK002 ability to remove both eosinophils and mast cells, given that Siglec-8 receptors are found on the surfaces of both. If AK002 only works on one cell type, it calls the entire Siglec-8 inhibition story into question. Allakos' CEO has described eosinophils and mast cells as partners in the "inflammatory cascade," suggesting that removing both is key to symptom reduction.



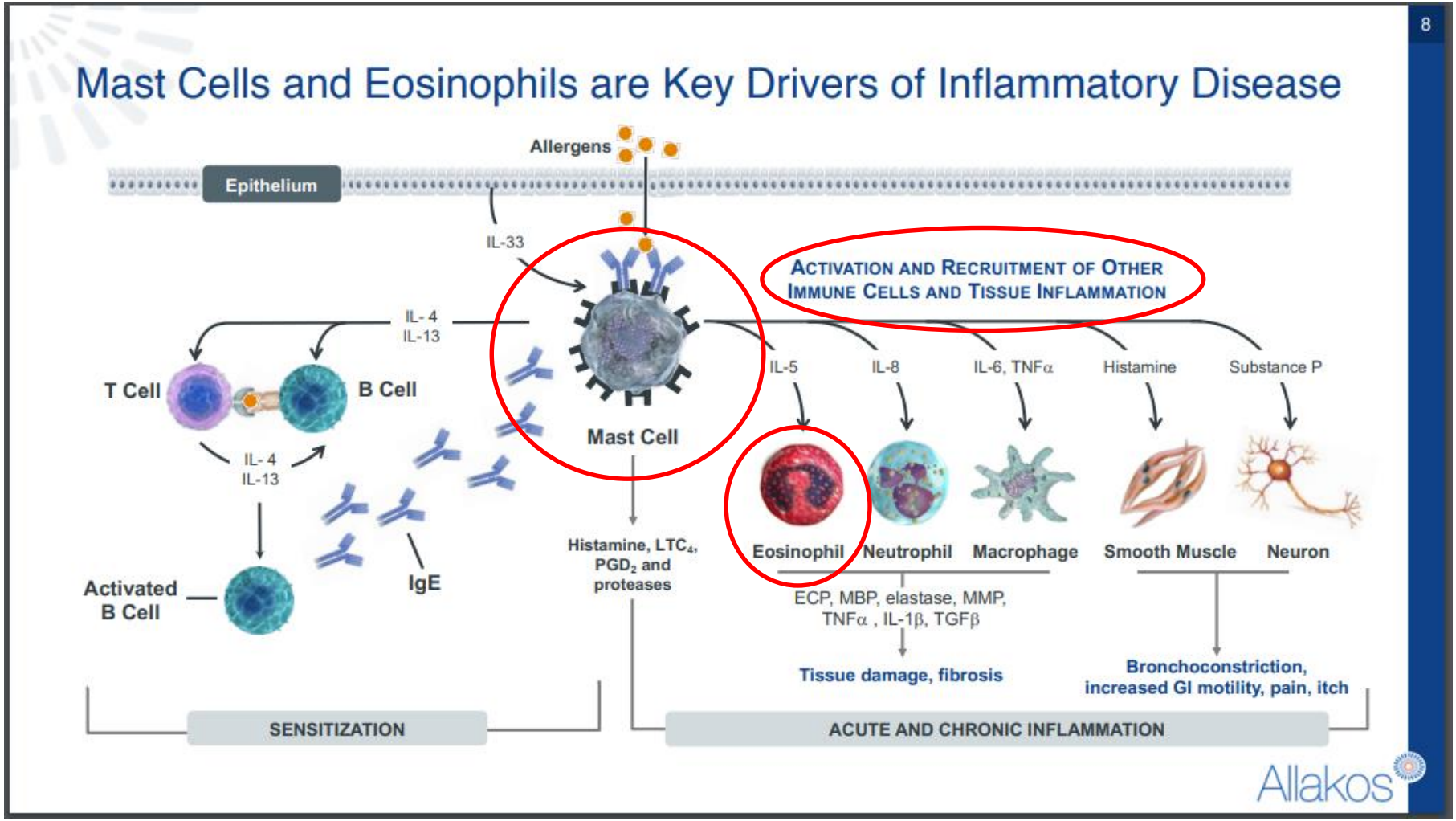
"So what we're trying to do with AK002 is to ***take mast cells and the eosinophils out of the equation. And by doing that, we would disrupt the inflammatory cascade and allow the tissues to calm down and heal."***

"Mast cells are similar to eosinophils and probably even, in some cases, worse *because they can be activated in more ways than an eosinophil can. And in particular, you see in the -- I think what's particularly important in atopy is the involvement of IgE activating the mast cell. So it's not surprising, I think, to us that* ***we see the activity in these comorbid conditions because they are substantially driven by mast cells and the eosinophils.*** *They're driven by other cells there, too, potentially. But what we're doing here and what we hypothesized and what appears to be being borne out in the data is* ***if we can remove these 2 cell types by killing EOs and by broadly inhibiting mast cells, then we can interrupt the inflammatory cascade****. And you can see a benefit to patients not only symptomatically but you're actually seeing healing of the tissue." – ALLK CEO, May 7, 2019*

Source: : https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; Allakos allergic conjunctivitis trial results call, CIQ/Bloomberg transcripts

Warning sign #19: The mystery of the missing mast cell data

Allakos' EG/EGE results presentation even features a mast cell prominently in the very center of a chart on the inflammatory process, to emphasize that it is mast cells which drive the "activation and recruitment" of other cells like eosinophils – creating a major problem for Allakos investors if AK002 fails to inhibit mast cells.



Source: : https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

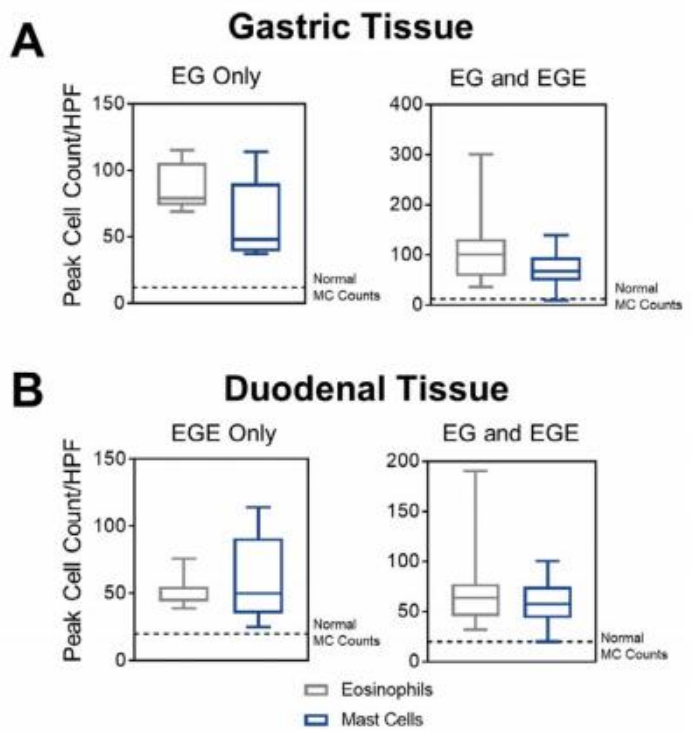
Warning sign #19: The mystery of the missing mast cell data

An abstract based on screening data from Allakos' ENIGMA study states that 97% of EGE/EGE patients had "markedly elevated" mast cell counts in addition to eosinophils, and that treatments "may need to target both cell types for optimal effect."

MAST CELLS IN ADDITION TO EOSINOPHILS ARE MARKEDLY ELEVATED AT BASELINE IN PATIENTS WITH EOSINOPHILIC GASTRITIS AND/OR GASTROENTERITIS

Evan S. Dellon, Kathryn A. Peterson, Robert M. Genta, Joseph A. Murray, Nirmala Gonsalves, Mirna Chehade, Marc E. Rothenberg, Paneez Khoury, Adam C. Bledsoe, Bhupinder Singh, Alan T. Chang, Bradford Youngblood, Henrik S. Rasmussen, Ikuo Hirano

(Figure 1B). **CONCLUSIONS:** In this interim dataset from the screening phase of the largest randomized EG/EGE study to date, we found that in addition to GI eosinophilia, MC counts were markedly and consistently elevated in gastric and duodenal tissue in symptomatic patients with isolated EG or EGE and in patients with overlapping EG and EGE. These data suggest a pathogenic role for both MCs and eos in EGIDs and that treatments for EGIDs may need to target both cell types for optimal effect.



Source: https://www.gastrojournal.org/article/S0016-5085(19)38721-9/pdf; red ours for emphasis.

Warning sign #19: The mystery of the missing mast cell data

Yet given the centrality of mast cells to the Allakos story, the company's pattern of withholding data on AK002's inhibitory effects on mast cells mirrors the lack of disclosure on eosinophil counts. Both the mastocytosis and allergic conjunctivitis trials listed basophil counts as an endpoint, yet the trial results press releases don't even mention the word basophil. Basophils are similar to mast cells and express Siglec-8. More importantly, the mastocytosis trial listed serum tryptase levels as an additional endpoint – yet Allakos has remained silent on whether AK002 impacted tryptase levels. Tryptase is contained only within mast cells and is the gold standard for measuring mast cell activity.

Phase 1 trial in indolent systemic mastocytosis - endpoints

2. Evaluate the change from baseline in absolute peripheral counts of eosinophils and basophils. [Time Frame: Through out the study from screening to Day 85 or early term visit]
3. Evaluate the change from baseline in serum tryptase and eosinophil grande protein levels. [Time Frame: Through out the study from screening to Day 29 or early term visit]

Source: ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT02808793?term=allakos&rank=7

Phase 1 trial in conjunctivitis - endpoints

Secondary Outcome Measures :

1. To evaluate the pharmacodynamics of AK002 in patients with AKC, VKC, or PAC as measured by changes from baseline in absolute peripheral blood counts of eosinophils and basophils [Time Frame: Starting pre-dose on day -1 to day 309 or early term visit]

Source: ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT03379311

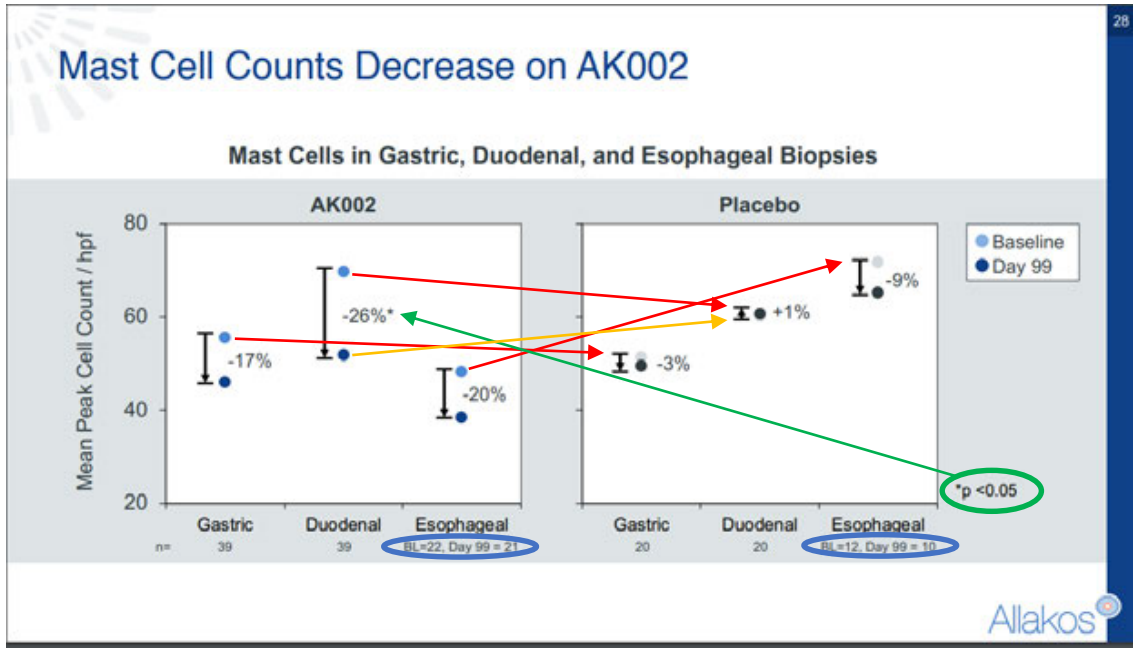
Source: https://en.wikipedia.org/wiki/Tryptase; red ours for emphasis.

Warning sign #19: The mystery of the missing mast cell data

The first time we see meaningful mast cell data from Allakos is in the August 5th EG/EGE results presentation, and it explains Allakos' reticence: AK002 failed to show statistical significance in mast cell reductions in two of three biopsy measures. Only duodenal biopsies showed activity, but the data is troubling and raises more questions than answers. We note the misleading presentation: showing bars that suggest strong response rates, with only an asterisk and P-value in tiny font to de-emphasize the lack of statistical significance.

Baseline levels between the two arms are divergent (red arrows ours)

Only duodenal counts show statistical significance (green emphasis)



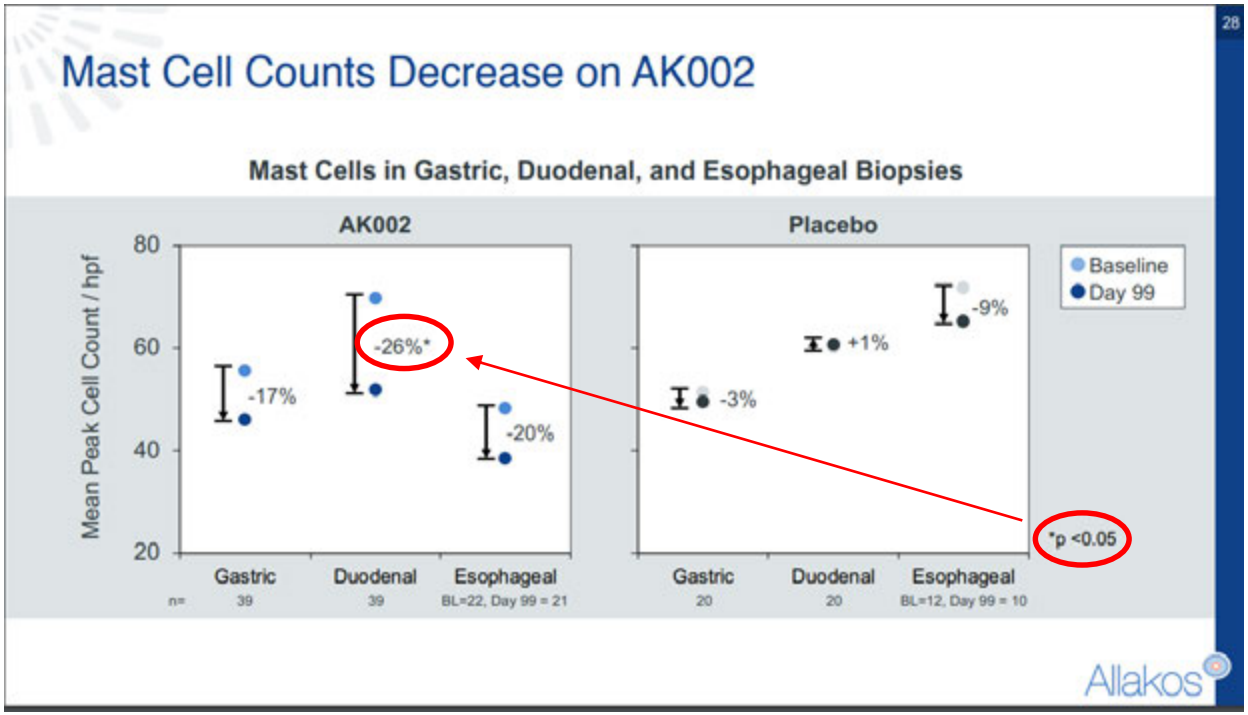
Duodenal baseline is much higher, yet day 99 appears a mere 5 cells/hpf lower than placebo (orange arrow)

Why are esophageal biopsies missing on day 99? (blue circles)

Source: : https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red, green, orange, and blue (circles only) ours for emphasis.

Warning sign #19: The mystery of the missing mast cell data

Despite the slide's attempt to steer investors to "effect size," it already reveals that AK002 failed to show statistical significance in two of three measures. We note other red flags as well. Only the p-value for duodenal tissue was stat sig. We find it stunning that Allakos doesn't even state whether the p-value refers to the low or high dose arm. If it was only the low dose arm, that would raise alarming questions and throw another wrench into the story. Given that the table of p-values shared on page 24 of the EG/EGE results deck uses 4 significant digits, why is the p-value on this page only disclosed as a threshold value, i.e., "*p<..05"? The threshold for stat sig if .05, and the gimmick below leads us to worry it may only barely be below .05 – technically stat sig but irrelevant, and a red flag suggestive of data manipulation.



Source: : https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #19: The mystery of the missing mast cell data

Several clinical trial design experts and scientists we consulted echoed these concerns, stating that "obviously something is wrong with this data", that it exhibits "consistent problems", and that it's "sketchy" and not "publishable."

"It doesn't make any sense why the placebo and active group baselines would be so different. The placebo baseline is higher. ***If I were in a lab running an experiment I'd scrap this data. Obviously something is wrong with it. There's no baseline control.*** *The esophageal baseline looks about 48. The placebo is over 70. And why did patients drop out? Mast cells are now suddenly not the story."* ***– Research scientist***

"They show percent changes on this page but not P values. Why? Because only one P value is statistically significant and they put it in tiny font at bottom of page. ***This page shows AK002 doesn't work well on mast cells****. It shows only a 20% change in mast cells. And the only one that's statistically significant is in the duodenum, not the gastric or esophageal mast cell counts.* ***There are consistent problems throughout the presentation. It's sketchy. You couldn't do this for a clinical publication. This would not be publishable because you can't draw conclusions from it."*** ***– PhD/Scientist who conducted due diligence at one of the largest biotech companies***

Source: Seligman expert consultations

Warning sign #19: The mystery of the missing mast cell data

Investors should not be surprised by these concerns, as we believe that Allakos is sitting on other data which conclusively demonstrates that AK002 is a flop. We note an Allakos poster which appears to be from 2018 based on the date in the URL – which states that "consistent with previous experiments" AK002 failed to reduce mast cells in ex vivo patient bone marrow despite Siglec-8 being "robustly expressed on diseased mast cells" in the samples. The chart appears to show that mast cell counts actually increased following AK002. "Ex vivo" means bone marrow aspirate removed from patients and cultured in a controlled laboratory setting with AK002 – a scenario with a far easier hurdle than demonstrating activity inside the body.

Figure 4. AK002 Significantly Reduced Eosinophils in ex vivo SM Patient Bone Marrow

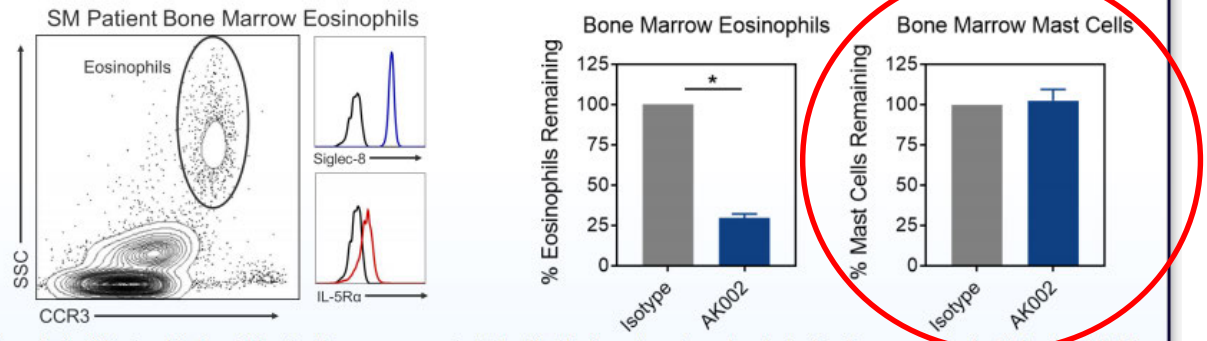


Figure 6: (Left) Eosinophils from SM patient bone marrow aspirate identified by flow cytometry and analysis of surface expression for Siglec-8 and IL-5Rα compared to a fluorescence minus one (FMO) control (black). (Right) Bone marrow aspirate from SM patients was cultured overnight with either an isotype control mAb (gray) or AK002 (blue) and eosinophils or mast cells were quantified the following day by flow cytometry. Eosinophils were gated on viable, CD45+, CD117-, CD16-. SSC^{Hi}, CCR3+; Mast cells were gated on viable, CD45+, CD117+, FcεRI+; Data shown are mean +/- SD from 3 SM patients; *p<0.05

- Siglec-8 is highly expressed on mature bone marrow eosinophils from SM patients
- AK002 significantly reduced ex vivo bone marrow eosinophils, but not mast cells, from SM patients consistent with previous experiments

Source: https://www.allakos.com/file.cfm/59/docs/Allakos_ASH_poster_2018_ISM_Ex_Vivo.pdf; red ours for emphasis.

Warning sign #19: The mystery of the missing mast cell data

Irrespective, the mast cell counts shown in the EG/EGE results are meaningless. The only relevant - and industry-standard measure - of mast cell activity and inhibition is tryptase levels, measured by a simple blood test. We find Allakos' redirection to mast cell counts vs. activity to be a tactic that would never fly with peer-review or the FDA. We suspect Allakos soured on talking about tryptase levels after their inclusion as an endpoint in the mastocytosis study, only to see the biomarker prove AK002 to be a failure.

TABLE III. Clinically available and validated markers of mast cell activation

Marker	Comment
Tryptase	The most specific marker Almost always increased in patients with hypotensive mast cell activation episodes Must be measured within 4 h of an episode and compared with baseline values Increased baseline levels in the absence of renal disease or myeloid neoplasm might indicate mastocytosis or familial hypertryptasemia
Urinary histamine metabolites	Fairly specific for mast cell activation Might be influenced by diet or bacterial contamination Specific cutoffs for mast cell activation syndrome not established
Urinary prostaglandin D_2 or metabolites	Increased in patients with mast cell activation Not specific to mast cells Specific cutoffs for mast cell activation not established Not recommended as the single marker of mast cell activation Can guide the decision to initiate aspirin therapy if the patient is not allergic to nonsteroidal anti-inflammatory drugs
Urinary leukotriene E_4	Increased in patients with mast cell activation Less clinical experience than other markers Might guide the decision to initiate leukotriene-targeting therapy

The second most specific biomarker for mast cell activation is urinary histamine metabolites.

Allakos' mastocytosis trial included these levels as an endpoint in addition to tryptase, and was silent on outcomes under this measure as well. Endpoint specified on ClinicalTrials.gov:

4. Measure changes form baseline in the 24-hour urine histamine metabolites.

Source: ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT02808793?term=allakos&rank=7

Source: https://www.jacionline.org/article/S0091-6749(17)31025-4/pdf; all red ours for emphasis.

Warning sign #19: The mystery of the missing mast cell data

The evidence strongly suggests that AK002 fails to inhibit mast cells, which calls the entire Allakos thesis into question. We conclude this section with comments from a research scientist and KOL that we consulted, who has studied mast cell biology for decades and is considered one of the world's top experts on their behavior. We find his feedback devastating: that it is mast cells which drive eosinophils to act up, and that Allakos' purported mast cell count reductions are "not significant, relevant, or clinical effects."

"Whenever eosinophils act up, it's mast cells that drive it. *Eosinophils live in blood not in tissue. They migrate into the tissue. The need a signal. Chemoattractant, complements, and other signals cause them to then adhere to the intraluminal side of vessels. Eosinophils sense they're needed and then migrate to the gradient.* ***Mast cells are good at releasing the signal that gets eosinophils into the tissue. The mast cells call for help."***

"It's all about inhibition of mast cell activation, not reducing their counts. *It's about a functional response. It is not about mast cell reduction. It's the chronic inflammation that drive the numbers."*

"If you decrease mast cell numbers by 15-20%, you will still have tissue that's the same in terms of inflammation*. Unless you reduce then in the skin by 99%, you still get a response when you activate then with a mast cell trigger on the skin. A few mast cells go a long way. You don't need 100 mast cells to get 100% of the response. Each cell punches above its weight.* ***The mast cell reductions shown in the EG/EGE results are not significant, relevant, or clinical effects."*** ***– Research scientist considered one of the world's top experts on mast cells***

Source: Seligman expert consultation

Warning sign #20: The ENIGMA tissue eosinophil reductions are suspiciously higher than shown in previous AK002 data from cell culture experiments and animal models. Allakos claims 97% reduction in tissue eosinophils, yet is reluctant to share blood eosinophil counts. In our opinion, the ENIGMA eosinophil reductions are simply too good to be true and fail the smell test – a sentiment shared by trial investigators.

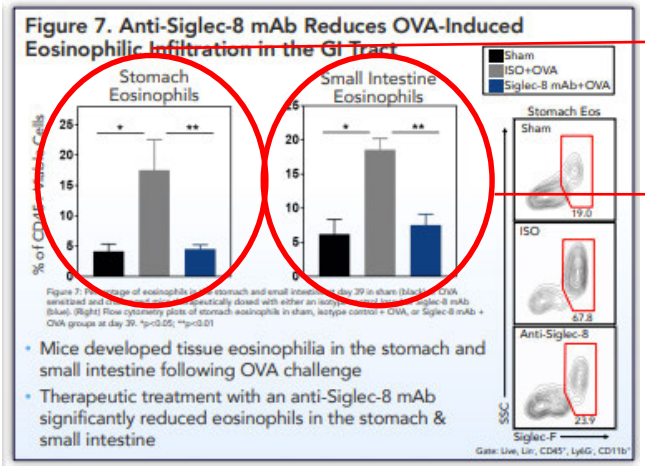
It's anomalous to see a compound perform better inside actual human patients than in carefully controlled and optimized in-vitro and ex-vivo studies which don't have the complex, unpredictable biochemistry of a real-world clinical setting.

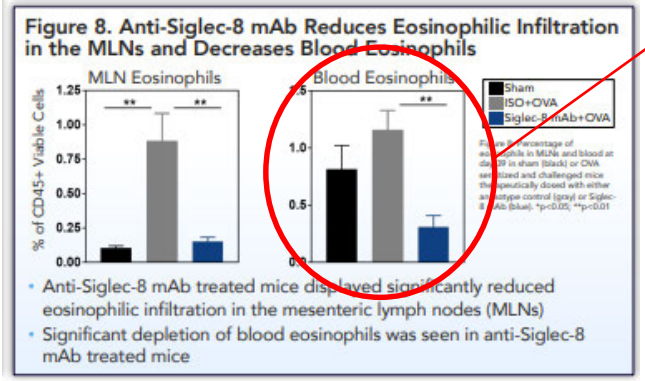
Allakos claims 97% reduction in tissue eosinophils but has withheld blood eosinophil counts. We have already noted that tissue levels were measured by a pathologist with a conflict of interest.

Warning sign #20: Tissue eosinophil reductions are suspiciously higher than previous AK002 lab data

The ENIGMA results indicated 97% mean reduction in tissue eosinophils in the high dose group and 92% in the low dose one. However, an Allakos poster which appears to be from 2018 shared data from mice bred to have eosinophilic gastritis and then treated with AK002. In comparison, eosinophils in mice appear to have decreased by only roughly 75%, 50%, and 75% in the stomach, small intestine, and blood, respectively – significantly lower rates.

- This study examines the activity of an anti-Siglec-8 mAb, murine AK002, in a mouse eosinophilic gastritis & gastroenteritis model





Stomach approximately 75% reduction

Small intestine approximately 50% reduction

Blood eosinophils approximately 75%

*All reductions as estimated by us from magnified chart

Source: https://www.allakos.com/file.cfm/59/docs/181004-1252-Allakos_EGE_2018_Mouse_Poster_4x6_FINAL.pdf; red ours for emphasis.

Warning sign #20: Tissue eosinophil reductions are suspiciously higher than previous AK002 lab data

Another Allakos poster, which also appears to be from 2018, shared data on eosinophil reductions in bone marrow tissue removed from patients and then cultured overnight with AK002. The data appears to show a only a ~70% reduction in eosinophils, again lower than the 92-97% reductions in the EG/EGE study. Allakos states below that "Siglec-8 is highly expressed" on the cells that were cultured. We wonder why AK002 was less effective ex vivo than in vivo, given that these cells appear to the perfect target for a Siglec-8 antibody and were presumably flooded with AK002 at concentrations and for a duration that are unrealistic for actual patients.

Figure 4. AK002 Significantly Reduced Eosinophils in ex vivo SM Patient Bone Marrow

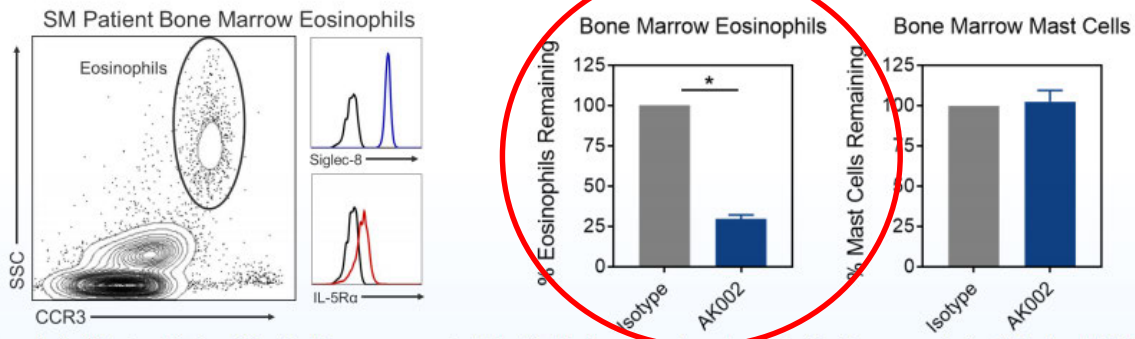


Figure 6: (Left) Eosinophils from SM patient bone marrow aspirate identified by flow cytometry and analysis of surface expression for Siglec-8 and IL-5Rα compared to a fluorescence minus one (FMO) control (black). (Right) Bone marrow aspirate from SM patients was cultured overnight with either an isotype control mAb (gray) or AK002 (blue) and eosinophils or mast cells were quantified the following day by flow cytometry. Eosinophils were gated on viable, CD45+, CD117-, CD16-. SSC^{Hi}, CCR3+; Mast cells were gated on viable, CD45+, CD117+, FcεRI+; Data shown are mean +/- SD from 3 SM patients; *p<0.05

- Siglec-8 is highly expressed on mature bone marrow eosinophils from SM patients
- AK002 significantly reduced ex vivo bone marrow eosinophils, but not mast cells, from SM patients consistent with previous experiments

Approximately 75% reduction

*As estimated by us from chart

Source: https://www.allakos.com/file.cfm/59/docs/Allakos_ASH_poster_2018_ISM_Ex_Vivo.pdf; red ours for emphasis.

Warning sign #20: Tissue eosinophil reductions are suspiciously higher than previous AK002 lab data

As another suspicious data point, Allakos' patent shows in-vitro data for blood eosinophil reductions in the range of roughly 80-85%. We wonder why the company's phase 2 study in healthy volunteers showed 100% elimination of blood eosinophils within one hour, yet dunking eosinophils in Siglec-8 antibodies for 16 hours in a lab did not.

(12) **United States Patent**
Bebbington et al.

(10) **Patent No.: US 9,546,215 B2**
(45) **Date of Patent: Jan. 17, 2017**

(54) **ANTI-SIGLEC-8 ANTIBODIES AND METHODS OF USE THEREOF**

(71) Applicant: **Allakos Inc.**, San Carlos, CA (US)

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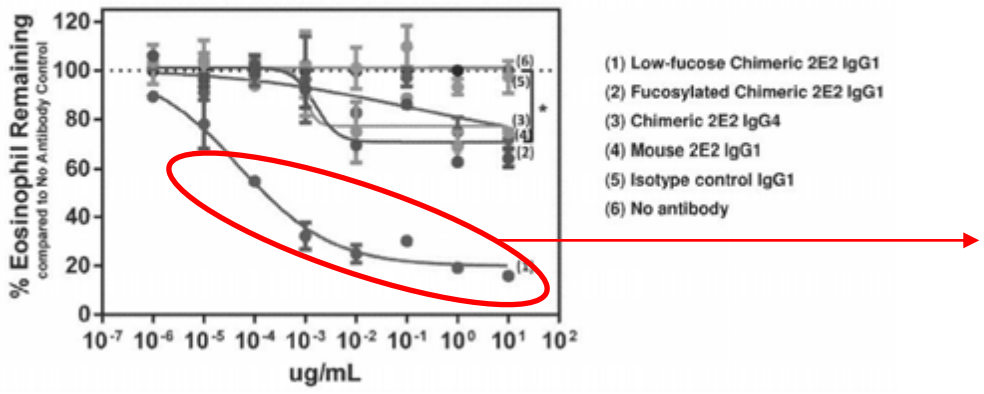
5,648,237 A 7/1997 Carter et al.
5,648,260 A 7/1997 Winter et al.

FIG. **7** is a graph showing killing of eosinophils with anti-Siglec-8 antibodies. Total peripheral blood leukocytes were incubated in the presence of the indicated anti-Siglec-8 and control antibodies concentrations for 16 hours. Reduction of eosinophil numbers were monitored by flow cytometry and quantified as a loss of CD16-negative IL5Rα+ cells with high side-scatter (SSC^{HI}).



Approximately 80-85% reduction

*As estimated by us from chart

Source: https://patentimages.storage.googleapis.com/cf/56/74/4d8edce6d6fc6f/US9546215.pdf; red ours for emphasis.

Warning sign #20: Tissue eosinophil reductions are suspiciously higher than previous AK002 lab data

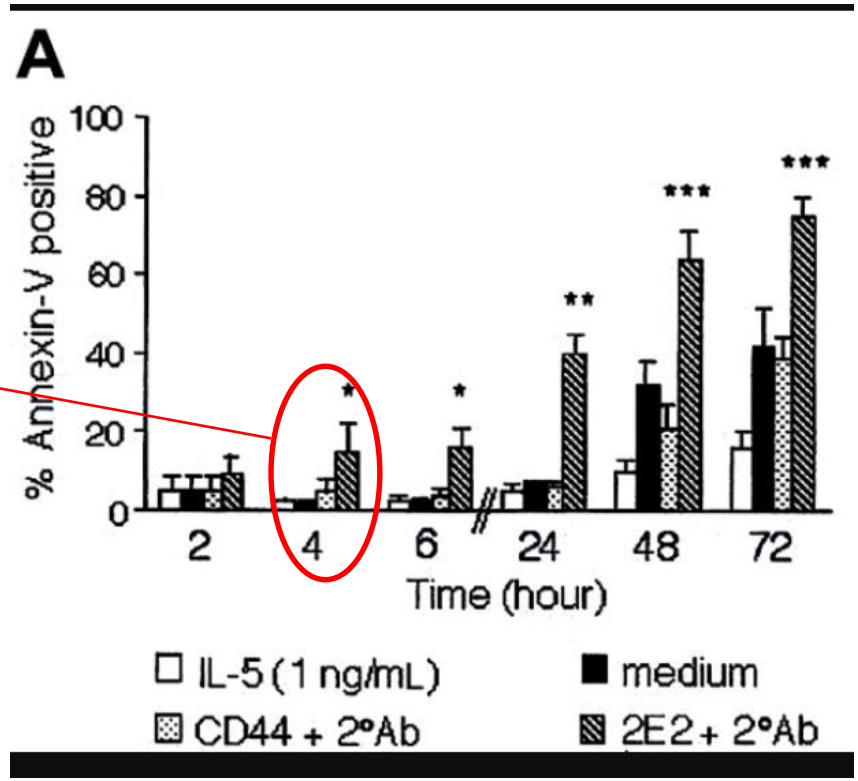
We further note a paper by Bruce Bochner, listed on the Allakos site as a co-founder and a member of their scientific advisory board since 2012, and upon whose research Allakos is based. The paper was cited in the Allakos patent and describes cell culture experiments using Siglec-8 antibodies on blood eosinophils. The paper indicates lower reductions than those claimed by Allakos in its phase 2 healthy volunteers study. We wonder how that trial showed 100% elimination within one hour, yet the company's co-founder showed only a 15% reduction in cell culture after four hours.

Ligation of Siglec-8: a selective mechanism for induction of human eosinophil apoptosis

Esra Nutku , Hideyuki Aizawa , Sherry A. Hudson , Bruce S. Bochner

Blood (2003) 101 (12): 5014-5020.

Figure 3A demonstrates a significant increase ($P \leq .005$) in annexin-V$^+$ eosinophils as early as 4 hours of culture with Siglec-8 cross-linking (15% ± 7%), compared with CD44 control cross-linking (5% ± 3%) or medium control (3% ± 1%), indicating a rapid apoptotic effect



Source: https://ashpublications.org/blood/article-lookup/doi/10.1182/blood-2002-10-3058; red ours for emphasis.

Warning sign #21: Even if one assumes AK002 isn't a P3 flop, it's commercial future is bleak as a me-too late-mover drug in a crowded space. Investigators stated that 6-8 hour infusions, monthly for life, render it dead-on-arrival. A realistic EG/EoE TAM implies at most $100-200MM in AK002 US sales. Influential ENIGMA investigators were devastating in stating that AZN's benralizumab and REGN's dupilumab are far ahead, and pointed to a long list of competing EoE/EG trials that ALLK investors appear unaware of. We encourage investors to study recent P2 data for dupilumab (Oct 2019) and benralizumab (Apr 2019) – stronger than AK002's ENIGMA results - and to watch for upcoming data from competing trials.

One investigator stated that no office is going to find nurses to sit through 8 hour infusions, and a journal article confirmed the 8-hour time, which made it "challenging" to enroll patients.

KOL comments indicate that a GI doctor may encounter only 10 EG cases over their entire career. The only theoretical commercial opportunity for Allakos is therefore in EoE, for which it hasn't even conducted a trial and for which the teaser data from ENIGMA is troubling. Although the EoE market appears optically larger with ~100k potential patients, a paper by an ENIGMA principal investigator states that 60-90% of patients achieve remission with dietary changes, and that 25-80% of patients achieve symptom resolution with cheap OTC PPI pills like Prilosec.

ENIGMA investigators indicate that ALLK's space is crowded and described formidable competitive headwinds facing AK002. Ominously for Allakos, Astra Zeneca received orphan drug designation for benralizumab in EoE on August 28, 2019 – just a few weeks after ALLK's ENIGMA topline release.

Warning sign #21: AK002's commercial future is bleak

ENIGMA trial investigators indicated that the long infusion times for AK002 render it commercially unviable. Doctors shared various figures for infusion length. Some reported 4 hours, others 8 hours, and stated that AK002 patients would need to sit through these infusions once a month for life. A KOL stated that this was the first infusion trial he had done, suggesting that EGID provider offices are not equipped for infusions. Another investigator said that no provider is going to find nurses to sit through 8 hour infusions. A journal article that interviewed investigators in another AK002 trial confirmed 8-hour infusions, which made it "challenging" to enroll patients.

"The infusion time made it challenging. Nurses are not available for hours *each time, every time…It was a significant length of time…****Which doctor is going to want to infuse when a nurse is $100 per hour? So if you infuse for 8 hours, that's $800. It's hard to find a nurse willing to infuse for 8 hours.*** *That's the hard part.* ***Insurers won't pay for it****…Patients aren't dying because of this condition."* ***– ENIGMA trial investigator***

"We haven't talked about the IV business. ***That's a big factor here. People don't want to take IV medications especially when they have other medications available. Dupixent and benralizumab are subcutaneous.*** *Right now Allakos is on an IV push.* ***A 4 hour infusion once a month is not going to be well-received****."* ***– ENIGMA trial investigator and prominent KOL in the EGID space***

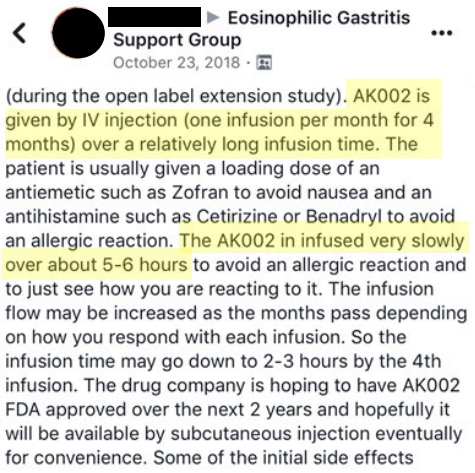
"The infusion was 4 hours. ***This was the first infusion trial we've done. Patients would have to come in for 4 hours once a month for life."*** ***- ENIGMA trial investigator also an influential KOL***

"Allakos' ***Phase IIa AK002 trial*** *in chronic spontaneous urticaria (CSU)* ***had challenging enrolment [sic] criteria, two investigators said, with one citing long study visits****…****The low patient numbers were due to the study requirement of patients having up to eight hours intravenous (IV) AK002 administration, said the investigator.*** *The long hours also meant that many patients failed screening, the investigator said. ClinicalTrials.gov does not cite the duration of study visits…"* ***– Pharmaceutical Technology 1/8/19***

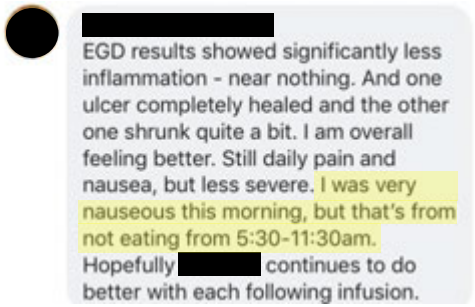
Source: Seligman expert consultations; https://www.pharmaceutical-technology.com/comment/chronic-urticaria-clinical-trial/

Warning sign #21: AK002's commercial future is bleak

Long infusion times are further corroborated by Facebook posts indicating 5-6 hour infusions.



*"AK002 is given by IV injection…over a relatively long infusion time…**The AK002 is infused very slowly over about 5-6 hours…"** – **Facebook post by parent of trial participant***



*"I was very nauseous this morning, but that's from not eating **from 5:30-11:30am."** – **Facebook post by trial participant***

Source: Facebook posts, "Eosinophilic Gastritis Support Group" https://www.facebook.com/groups/258285487951166/

Warning sign #21: AK002's commercial future is bleak

Investigators further pointed to the puny size of the eosinophilic gastritis market. One stated that a GI doctor may encounter only 10 EG cases over their entire career. Another, one of the most influential KOL's, implied ~7,000 total patients. Similar, competing drugs in the eosinophilic class such as IL-5's - benralizumab (Fasenra), mepolizumab (Nucala), reslizumab (Cinqair) – or dupilumab (Dupixent) are list-priced at ~$30K/year in year one and lower thereafter. Even if AK002 works, its pricing is therefore a given, implying a domestic EG market size of barely ~$200MM at 7k cases, assuming 100% of patients are diagnosed and 100% of them fail dietary and other treatments – after those adjustments the actual TAM could easily be <$50MM. However, we note an analysis by the influential Institute for Clinical and Economic Review (ICER), pegging the value of an anti-eosinophilic drug like Nucala at only $8-12K/year, suggesting downward price pressure from insurers.

"This was a hard trial to recruit for. There's a low incidence of this disease. Over their lifetime, a typical GI doctor will see 10 cases if they're lucky*….The rate of these diseases is very low."* ***– ENIGMA trial investigator***

"Eosinophilic gastritis is a rare disease. ***Probably about 1 person out of 40-50k people has it****. The data is not conclusive."* ***– ENIGMA trial investigator/KOL***

"Nucala, an injectable indicated for severe asthma patients with eosinophilic inflammation, should cost between $7,800 and $12,000 per year*, according to an analysis by the Institute for Clinical and Economic Review (ICER).* ***That's as much as 76% lower than the $32,500 tag it bears right now."*** ***– FiercePharma, 12/22/15***

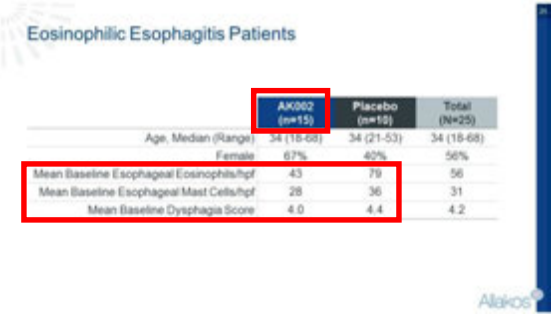
Table 4.17. Base-Case ICER and Annual Price (side-by-side)

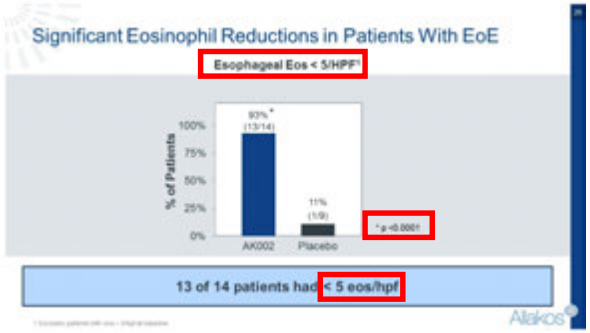
	Base-Case ICER	Annual Price	Notes
Omalizumab	$313,000	$28,900	Manufacturer provided net price
Mepolizumab	$344,000	$29,500	Manufacturer provided net price
Reslizumab	$412,000	$30,500	FSS price
Benralizumab	$412,000	$30,800	FSS price
Dupilumab	$464,000	$36,000	Used FDA approved dosing and FSS price

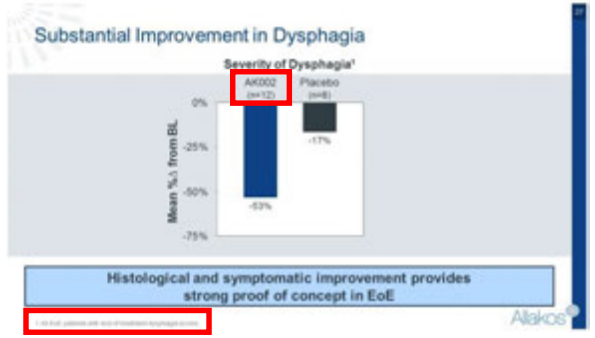
Source: Seligman expert consultations; https://icer-review.org/wp-content/uploads/2018/04/ICER_Asthma_Draft_Report_092418v1.pdf; https://www.fiercepharma.com/sales-and-marketing/gsk-s-new-32-500-asthma-med-costs-at-least-2x-too-much-u-s-pricing-watchdog

Warning sign #21: AK002's commercial future is bleak

The only theoretical commercial opportunity for Allakos is therefore in eosinophilic esophagitis (EoE), for which it hasn't even conducted a trial. ALLK shared teaser data from ENIGMA for a subgroup of patients with concomitant EoE. Only 15 patients on AK002 had EoE, and the data is a farce for reasons previously discussed: 1) AK002 patients started with significantly lower baseline eosinophil and mast cell levels, and less severe symptoms, than placebo (p.); 2) a mysterious claim of dysphagia reduction – the signature symptom of EoE – as the fatally flawed PRO didn't even include dysphagia as a symptom; 3) alarming data discrepancies as p-values for esophageal eosinophil reduction keep changing, similar to the stomach eosinophil data (p.); and 4) the dysphagia data includes only 12 AK002 patients – excluding 3 patients of the total – which suggests cherry-picking.







N=15 in AK002 EoE subgroup, yet dysphagia improvement slide on far right uses N=12 with no explanation beyond a cryptic footnote*: "[1]All EoE patients with end of treatment dysphagia scores."*

Multiple versions of this slide with different p-values and different thresholds for defining eosinophil reduction

How were dysphagia scores measured if the PRO didn't even include the symptom?

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156459019028522/allk-ex991_7.htm; red ours for emphasis.

Warning sign #21: AK002's commercial future is bleak

The clinical literature suggests an EoE prevalence of 10-57 cases per 100k people, or about 100K cases domestically at the midpoint[1]. However, most patients achieve remission with dietary management, as many KOL's view EoE as a food allergy condition. A paper by Evan Dellon, a Principal Investigator for the ENIGMA trial, indicates "remission with response rates above 90%" with a restrictive diet, and 60-90% with a less restrictive diet with easier adherence[2]. Another paper by Dellon indicates that 25-80% of patients achieve symptom resolution with proton pump inhibitors (PPI's) and 33-61% achieve histologic resolution – roughly 50% average across both measures[3]. PPI's like Prilosec are available generically and OTC for less than $30/mo. The difference between EoE and run-of-the-mill reflux remains of topic of clinical debate, and PPI trials are a mainstay of EoE treatment[4]. A simple but generous TAM calculation yields a US market size of only $420MM, before even accounting for the ubiquity of steroids and the crowded nature of the EoE space. Even if ALLK captured 1/3 of the pie, we fail to see how AK002 drives more than $100MM in US EoE sales.

EoE total addressable market calculation			
Methodology		**Assumptions**	
Epidemiological prevalence of EoE, domestically	112,000	Clinical literature indiciates 10-57 cases/100k, or 34/100k on avg	
Percent of epidemiologic population actually dagnostoed with EoE	50%	Generous assumption given few specialists, and clinical diagnosis requires BOTH endoscopay and biopsy	
Total diagnosed cases	56,000		
Less: Patients managed successfully by diet	28,000	Assume 50%, a generous assumption given 60-90% response rate in the clinical literature	
Equals: Remaining potential EOE patients	28,000		
Less: Remaining potential EOE patients managed by PPI	14,000	Clinical literature indicates about 50% success rate	
Equals: Remaining potential EoE patients prior to steroids, IL5, etc.	14,000		
Total addressable market @ $30k/year per patient	**$420,000,000**		

Source: [1]https://www.ncbi.nlm.nih.gov/pubmed/29129296; [2]https://med.virginia.edu/ginutrition/wp-content/uploads/sites/199/2018/04/EoE-April-18.pdf; [3]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4302490/; [4]https://www.ncbi.nlm.nih.gov/pubmed/28291175

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #21: AK002's commercial future is bleak

ENIGMA investigators indicate that ALLK's space is crowded, and one of the most influential KOL's in the space indicated that Astra Zeneca's benralizumab is already far ahead in important ways. We note the large number of studies in benralizumab - 59 per ClinicalTrials.gov - for a long list of eosinophilic indications, such as atopic dermatitis, COPD, eosinophilic asthma, hypereosinophilic syndrome, nasal polyps, and across different patient populations like pregnant women and children. Allakos clearly seems to know it's late to the eosinophil party, given its attempt to pick off a couple of niche indications. The effort strikes us an attempt to grab nickels in front an impending freight train of larger players who also have designs in EG/EoE.

"This is a pretty big landscape now*. AK002 and benralizumab have an identical mode of action expect siglec-8 presumably also targets mast cells.* ***Benralizumab is FDA-approved and is a solid, subcutaneous, safe medication****. It's well tolerated. It's approved in adolescents in asthma.* ***The drug is already doing younger people so it's far ahead****. They already have a lot of patient exposures. Tens of thousands have been exposed."*

"That's the big question, can AK002 show a benefit compared to benralizumab? I'm not going to say in public I don't believe the AK002 data."

*"****Then there are other drugs like dupilumab.*** *It's already has approval for three different types of allergies and* ***they're moving full speed ahead in EG and EoE****. EG is already in clinical trials.* ***Those will be the players and they're ahead. There will be others in next five years."***

-ENIGMA trial investigator and KOL

Source; Seligman expert consultations

Warning sign #21: AK002's commercial future is bleak

Another influential ENIGMA investigator walked us through competing trials in EoE, and described the formidable competitive headwinds facing AK002, stating that "this has quickly become a more crowded space over the last two years." This investigator felt that Regeneron's dupilumab was already furthest ahead among biologics.

"This has quickly become a more crowded space over the last two years. I don't know who's going to win. Dupilumab is furthest along biologics-wise*. Dupilumab has a phase 2 and phase 3 ongoing in EoE."*

"Celgene is planning a phase 3 for their anti IL-13 RPC4046 in EoE. *The phase 2 was published in Gastroenterology last fall."*

*"****Takeda has a phase 3 for an oral steroid suspension for EoE****. They're presenting at ACG."*

"Adare has a dissolvable tablet and are presenting phase 2 *next week in Europe. It's a steroid."*

"Jorveza by Falk Pharma *is approved in Europe, also a steroid."*

*"****The Regeneron dupilumab phase 2 in EoE was published last week. The phase 3 is ongoing****. It was published in Gastroenterology.* ***It was a very positive outcome****. The primary outcome was symptoms, and a very good histologic and endoscopic response. It was robust. There was a good decrease in eosinophils. Dupilumab was for esophagus not stomach."*

*"****Then you have IL-5's*** *like mepolizumab etc."*

-ENIGMA trial investigator and KOL

Source: [1]https://www.ncbi.nlm.nih.gov/pubmed/29129296; [2]https://med.virginia.edu/ginutrition/wp-content/uploads/sites/199/2018/04/EoE-April-18.pdf; [3]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4302490/; [4]https://www.ncbi.nlm.nih.gov/pubmed/28291175

Warning sign #21: AK002's commercial future is bleak

Ominously for Allakos, Astra Zeneca received orphan drug designation for benralizumab in EoE on August 28, 2019[1] – just a few weeks after ALLK's ENIGMA topline release. A prominent ENIGMA investigator explained why AK002's actual mechanism of action – ADCC, not apoptosis – is identical to benralizumab. We question how AK002 has any commercial relevance if 1) it's mechanism is the same as benralizumab and it doesn't even leverage siglec-8; 2) it requires a 6-8 hour infusion once a month for life, vs. benralizumab's superior mode of delivery – a subcutaneous injection every few months; and 3) it lacks the clinical and safety validation benralizumab has accumulated from extensive real-world usage.

"The whole story of siglec-8 in the literature is confusing. It goes back a long time, literally decades. *It was originally shown to be an inhibitory receptor on eosinophils, that they go into apoptosis. AK002 targets Siglec-8 on eosinophils.* ***It's clearly not working by apoptosis but by activating the immune system to kill the eosinophil. That's exactly how benralizumab works. Allakos clearly says the antibody they generate works by an ADCC mechanism.*** *When you look at the mechanisms of action, you need to know the difference"*

"The protein on the cell is called siglec-8. It's a receptor on the eosinophil. It's selective to eosinophils. It's only on eosinophils and mast cells. ***When AK002 was discovered, they said it caused eosinophils to die by apoptosis. Cell death.*** *There was a lot of research on that. The founders published articles.* ***But how AK002 really works is by causing the immune cells that clear things to kill the call. That mechanism is called ADCC.*** *So AK002 doesn't take advantage of anti siglec-8 activity. It doesn't take advantage of siglec-8 only being on eosinophils.* ***Benralizumab does exactly the same thing****. It causes ADCC against eosinophils,. It works well.* ***I was surprised when AK002 developed this drug because it didn't take advantage of siglec-8 activity. It's just standard ADCC."*** ***– ENIGMA trial investigator and KOL***

Source; [1]https://www.astrazeneca.com/media-centre/press-releases/2019/fasenra-granted-us-orphan-drug-designation-for-eosinophilic-oesophagitis-28082019.html ; Seligman expert consultations

Warning sign #21: AK002's commercial future is bleak

We encourage investors to read the results of AZN's phase 2 benralizumab trial published in the New England Journal of Medicine in April 2019, especially the 54-page data appendix, as the contrast highlights the omissions, cherry-picking, and superficial endpoints that characterize Allakos' behavior. Subcutaneous injections of benralizumab produced superior eosinophil reduction than AK002 – to undetectable levels in the blood, marrow, and tissue, in addition to succeeding on symptom improvement. We note ALLK suspiciously excluded histologic markers like blood eosinophils from its ENIGMA disclosure. Notably, the benralizumab trial included data for a subgroup with eosinophilic gastritis – which demonstrated superior tissue eosinophil reduction in EG patients than AK002. Benralizumab used a threshold of ≤1 eosinophil/hpf vs. ALLK's looser definition(s!) around 5 or 6/hpf. We fail to see how AK002 has any chance against benralizumab or other incumbents.

*"[Eosinophils] were undetectable in the blood, bone marrow, and tissues after 12 weeks of benralizumab therapy…**Tissue samples obtained at week 24 showed nearly complete depletion of eosinophils (≤1 eosinophil per high-power field)** in a total of 52 gastrointestinal biopsy samples obtained from the seven patients with gastrointestinal eosinophilia…."*

Table S3. Effect of benralizumab on gastrointestinal tissue eosinophilia

	Baseline (Pre-treatment)								Week 24 (Post-benralizumab treatment)							
	#6	#7	#11	#13	#14	#15	#16	Median (Range)	#6	#7	#11	#13	#14	#15	#16	Median (Range)
Proximal/Mid Esophagus	0	164	11	0	60	0	0	0 (0-164)	0	0	0	0	0	0	1	0 (0-1)
Distal Esophagus	1	>200	6	0	130	0	109	6 (0- 200)	0	0	0	0	0	0	0	0 (0-1)
Stomach	14	>200	17	22	143	1	>200	22 (1- 220)	0	0	0	0	0	0	1	0 (0-1)
Duodenum	--	43	90	53	59	18	4	48 (4-90)	3	0	1	0	0	0	0	0 (0-3)
Terminal Ileum	--	--	--	30	37	20	32	32 (20-80)	--	--	1	0	0	0	0	0 (0-1)
Colon, Ascending	82*	--	80*	>200	34	47	77	77 (34-200)	--	--	0	0	0	0	0	0 (0)
Colon, Transverse	--	--	--	168	20	37	53	53 (20-168)	--	--	0	0	0	0	0	0 (0-1)
Colon, Descending	--	--	--	134	10	33	37	37 (10-134)	--	--	0	0	0	0	0	0 (0-1)
Rectosigmoid	--	--	--	157	9	33	26	33 (9-157)	--	--	0	0	0	0	0	0 (0-1)

"Table S3. Effect of benralizumab on gastrointestinal tissue eosinophilia" shows essentially total elimination of eosinophils in esophageal and stomach/duodenal tissue

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa1812185; appendix: https://www.nejm.org/doi/suppl/10.1056/NEJMoa1812185/suppl_file/nejmoa1812185_appendix.pdf; red ours.

Warning sign #21: AK002's commercial future is bleak

We further encourage investors to read the results of Regeneron's P2 study for dupilumab in EoE, just published on October 5, 2019, and with an ongoing P3. We note that the paper is co-authored by many ENIGMA trial investigators, and a Principal Investigator of the Allakos study is listed as a lead author. In contrast to Allakos, the study used a robust set of endpoints and demonstrated strong results across symptom (using a battery of validated PRO's, unlike ALLK), histologic, tissue, endoscopic, and esophageal distensibility measures. Coming straight from Allakos' own trial investigators – and weeks after the ENIGMA results - the words are damning: "to our knowledge, dupilumab is the first targeted biologic agent to improve dysphagia, histologic and endoscopic measures of disease, and esophageal function and have an acceptable safety profile in adult patients with active EoE."

Efficacy of Dupilumab in a Phase 2 Randomized Trial of Adults With Active Eosinophilic Esophagitis

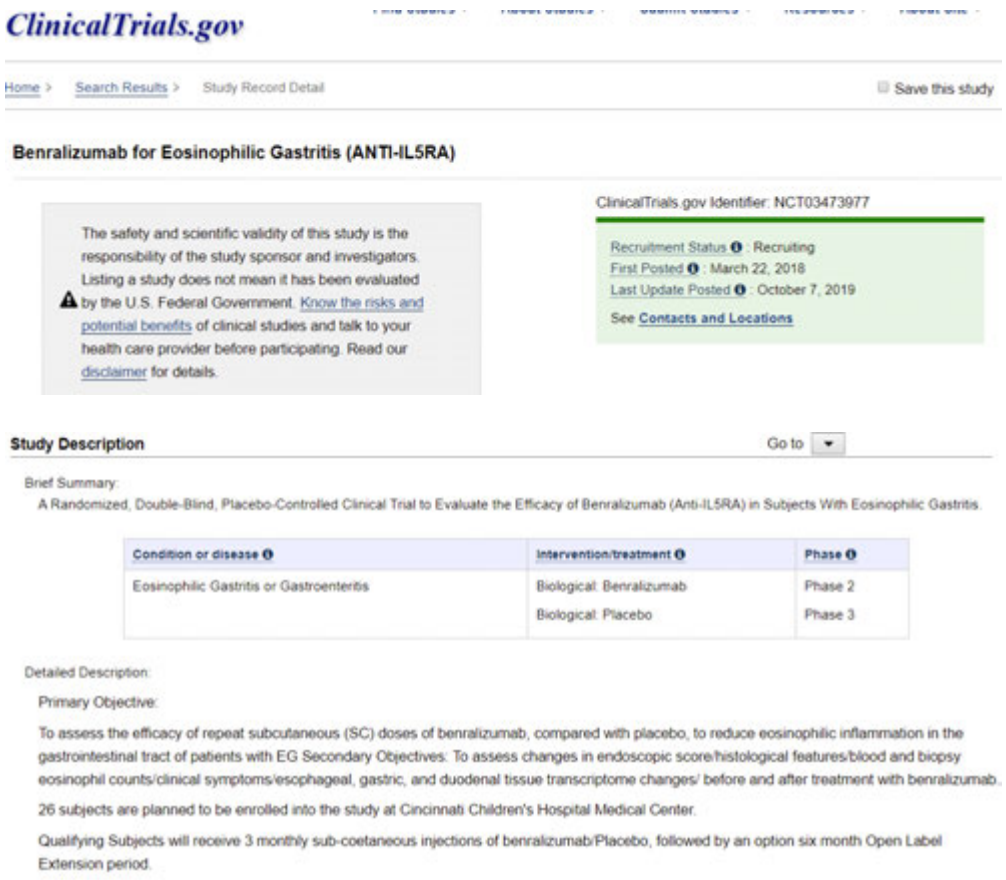
Ikuo Hirano,[1,*] **Evan S. Dellon**,[2,*] Jennifer D. Hamilton,[3] Margaret H. Collins,[4] Kathryn Peterson,[5] Mirna Chehade,[6] Alain M. Schoepfer,[7] Ekaterina Safroneeva,[8] Marc E. Rothenberg,[4] Gary W. Falk,[9] Yehudith Assouline-Dayan,[10] Qiong Zhao,[3] Zhen Chen,[3] Brian N. Swanson,[11] Gianluca Pirozzi,[11] Leda Mannent,[12] Neil M. H. Graham,[3] Bolanle Akinlade,[3] Neil Stahl,[3] George D. Yancopoulos,[3] and Allen Radin[3]

In conclusion, to our knowledge, dupilumab is the first targeted biologic agent to improve dysphagia, histologic and endoscopic measures of disease, and esophageal function and have an acceptable safety profile in adult patients with active EoE. Further studies are required to determine the long-term efficacy and safety of dupilumab in the treatment of EoE.

Source: https://www.gastrojournal.org/article/S0016-5085(19)41415-7/pdf; red ours for emphasis.

Warning sign #21: AK002's commercial future is bleak

The proliferation of competing EoE trials, by far larger companies with established drugs, is a critical problem for Allakos, as EoE is the only market with even arguable commercial relevance. EG is too small to matter, and we have already pointed to benralizumab data from April 2019 in the NEJM that shows superior stomach eosinophil reduction than AK002. Given the strength of this initial data, we remind investors of AZN's ongoing P2 trial for benralizumab specifically in EG, with likely data in early 2020. We further note the higher quality of the trial design, which encompasses a variety of symptom, histologic, endoscopic, and other endpoints in contrast to ALLK.



ClinicalTrials.gov

Home > Search Results > Study Record Detail

Save this study

Benralizumab for Eosinophilic Gastritis (ANTI-IL5RA)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03473977

Recruitment Status : Recruiting
First Posted : March 22, 2018
Last Update Posted : October 7, 2019

See Contacts and Locations

Study Description Go to

Brief Summary:
A Randomized, Double-Blind, Placebo-Controlled Clinical Trial to Evaluate the Efficacy of Benralizumab (Anti-IL5RA) in Subjects With Eosinophilic Gastritis.

Condition or disease	Intervention/treatment	Phase
Eosinophilic Gastritis or Gastroenteritis	Biological: Benralizumab	Phase 2
	Biological: Placebo	Phase 3

Detailed Description:

Primary Objective:

To assess the efficacy of repeat subcutaneous (SC) doses of benralizumab, compared with placebo, to reduce eosinophilic inflammation in the gastrointestinal tract of patients with EG Secondary Objectives: To assess changes in endoscopic score/histological features/blood and biopsy eosinophil counts/clinical symptoms/esophageal, gastric, and duodenal tissue transcriptome changes/ before and after treatment with benralizumab.

26 subjects are planned to be enrolled into the study at Cincinnati Children's Hospital Medical Center.

Qualifying Subjects will receive 3 monthly sub-coetaneous injections of benralizumab/Placebo, followed by an option six month Open Label Extension period.

Source: https://clinicaltrials.gov/ct2/show/NCT03473977

Warning sign #22: Allakos appears to have a pattern of not playing by the rules, beyond those pertaining to trials. In addition to making a mockery of biotech disclosure practices, compliance, and data integrity, we note 1) the suspicious timing of a recent option grant, which raises concerns of backdating and "spring-loading"; 2) apparent violation of rules for papers at medical conferences; and 3) questionable behavior with regard to Reg FD.

Seligman Investments | ALLAKOS (NASDAQ: ALLK)

Warning sign #22: Allakos appears to have a pattern of not playing by the rules

We begin with the suspicious timing of a recent option grant. A Form 4 filed on Tuesday, August 6th, disclosed an option grant to the CFO for 120k shares with an exercise price of $31. The form states that the grant date was two business days earlier, Friday, August 2nd. Note that the company released trial results on the day in between, and the stock went from $31 to $65 in one session, and tripled within two days. The stock was already in the $80's the day the form 4 was filed with an exercise price of $31.

Form 4 filed on Tuesday, August 6th

$31 exercise price

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
				Code	V	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares				
Stock Option (Right to Buy)	$31	08/02/2019		A		120,000		(1)	08/02/2029	Common Stock	120,000	$0.00	120,000	D	

Explanation of Responses:

1. Mr. Redmond was granted options to purchase 120,000 shares of common stock on August 2, 2019, of which 25% will vest on August 1, 2020, the first anniversary of the vesting commencement date, with the remaining 75% of the options vesting monthly in substantially equal installments over the following 36 months, subject to Mr. Redmond's continued services to the Company through each vesting date. The options will terminate on the tenth anniversary of the date of grant, unless otherwise previously terminated pursuant to the terms of the option agreement accompanying the grant.

"Mr. Redmond was granted options to purchase 120,000 shares of common stock on August 2, 2019…"

Source: https://www.sec.gov/Archives/edgar/data/1564824/000156761919015859/xslF345X03/doc1.xml; red ours for emphasis.

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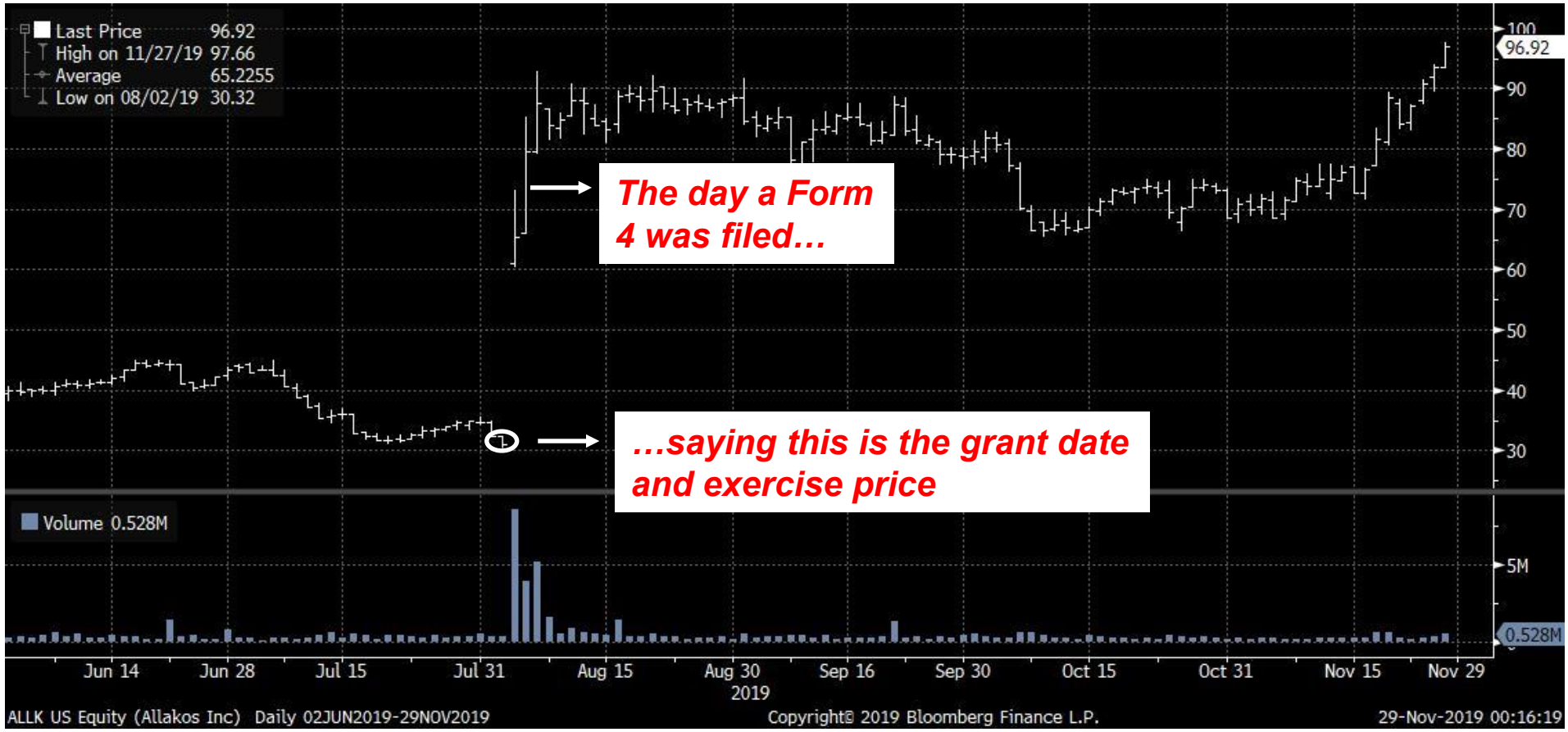
The sequence of events is self-explanatory.



Source: Bloomberg stock chart, SEC filings

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We note that the DOJ has criminally prosecuted executives for options backdating practices[1]. Misreporting the actual grant date to cherry-pick a lower strike price is a violation of both securities and tax laws, as well as corporate law pertaining to fiduciary duties. We do not know if Allakos misrepresented the actual grant data, and merely note the remarkably prescient timing without making an allegation of illegal behavior. Irrespective of options backdating considerations, we believe that this grant creates legal questions for Allakos executives and board members around the issue of "spring-loading" options – the dubious practice of granting options immediately prior to releasing favorable information. A key ruling in June 2019 by the Delaware Court of Chancery – against other biotech executives, no less - indicates the risk to directors and executives for breaching their "fiduciary duty of loyalty by misusing corporate information to…benefit themselves."[2]

"Delaware courts are beginning to analyze claims concerning the controversial practice of spring-loading options. Spring-loading is the granting of options just prior to the release of favorable company information (in the company's possession at the time of the grant). *The options are granted at a market price on the day of the grant. They are said to be 'spring-loaded' because upon release of the favorable news, the stock price is expected to rise and the options would then become 'in-the-money [..]* ***Three recent opinions of the Delaware Chancery court are significant because they confirm that spring-loading may give rise to a breach of fiduciary duty claim****…."* – *Lawyer Journal Newsletters,* http://www.lawjournalnewsletters.com/sites/lawjournalnewsletters/2008/04/25/spring-loading-options/

"Both of these cases represent strong pronouncements by the Delaware Court of Chancery that directors who backdate or spring-load options in violation of either the letter or the spirit of shareholder-approved option plans are likely to be found liable for breaches of the fiduciary duty of loyalty. *Additionally, the Court has recognized that a company (or its shareholders acting derivatively) can pursue claims for unjust enrichment against the recipients of the options, even if those recipients are not blameworthy in connection with the option timing itself."* – *Commentary by Delaware law firm,* https://www.gelaw.com/wp-content/uploads/2015/02/Option-Backdating-and-Spring-Loading.pdf

Source: [1]https://www.gibsondunn.com/wp-content/uploads/documents/publications/Farhang-BNABackdating-Directors.pdf; [2]https://www.jdsupra.com/legalnews/chancery-addresses-spring-loading-of-56433/

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Allakos appears to have a penchant for pushing the edge in other areas. Identical ENIGMA trial abstracts were submitted at two key medical conferences which occurred within a week of each others – UEG and ACG, where an investigator spoke on Oct 22 and 29, respectively. Medical conferences are based on the release of new data and most forbid the presentation of duplicate material. The copy and paste of UEG material at ACG a week later appears to flagrantly violate both conferences' rules.

UEG and ACG abstracts are a cut and paste…

UEG - Results: 59 patients were evaluable for efficacy (n=20 in HD; n=19 in LD; n= 20 in PBO). BL characteristics were balanced between groups. For the primary endpoint, the AK002 groups had an overall 95% mean reduction of tissue eos relative to BL compared to a 10% mean increase in PBO (p< 0.0001; Table 1). Tissue eos depletion to ≤6 eos/hpf was seen in 37 (95%) AK002 patients. There was significant improvement in TSS scores with AK002 compared to PBO (p=0.0012). Among all AK002 patients, 69% were treatment responders compared to 5% of PBO patients (p=0.0008). Among EG/EGE patients with concomitant EoE, significant histologic and substantial symptomatic improvements were reported with AK002 compared to PBO. The most common adverse events (AE) reported for AK002 were mild to moderate infusion related reactions (IRR), most common at the first infusion only. Treatment emergent serious AEs were similar between AK002 and PBO groups. There was one drug related serious AE, an IRR that resolved within 24 hours without sequelae.

Source: http://www.professionalabstracts.com/ueg2019/iplanner/#/grid/1571702400;

ACG - Results: 59 patients were evaluable for efficacy (n=20 in HD; n=19 in LD; n= 20 in PBO). BL characteristics were balanced between groups (Table 1). For the primary endpoint, the AK002 groups had an overall 95% mean reduction of tissue eos relative to BL compared to a 10% mean increase in PBO (p<0.0001). Tissue eos depletion to ≤6 eos/hpf was seen in 37 (95%) AK002 patients. There was significant improvement in TSS scores with AK002 compared to PBO (p=0.0012; Table 2). Among all AK002 patients, 69% were treatment responders compared to 5% of PBO patients (p=0.0008). The most common adverse events (AE) reported for AK002 were mild to moderate infusion related reactions (IRR), most common at the first infusion only. Treatment emergent serious AEs were similar between AK002 and PBO groups. There was one drug related SAE, an IRR that resolved within 24 hours without sequelae.

Source: https://www.eventscribe.com/2019/ACG/agenda.asp?pfp=Scientific&cf=Annual%20Scientific%20Meeting&sddo=0

…which appears to violate policies of both conferences

"Abstracts that will be published in a peer-reviewed journal before the ACG meeting may not be submitted."

Source: https://acgmeetings.gi.org/wp-content/uploads/2019/02/ACG2019-Abstract-Submission-Instructions.pdf

"The Author(s) warrant(s) to be the sole Author(s) of the abstract submitted and ***that it is an original work and has not been previously published in whole or to a substantial extent elsewhere."***

Source: https://acgmeetings.gi.org/wp-content/uploads/2019/02/ACG2019-Abstract-Submission-Instructions.pdf

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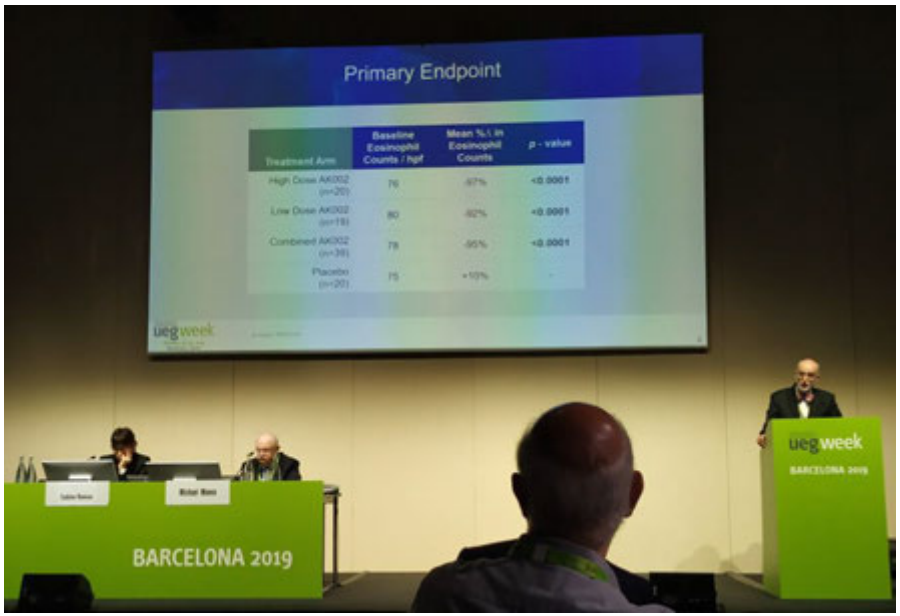
We further note behavior we find troubling with regard to Regulation FD, which "prohibits companies from selectively disclosing material nonpublic information…without concurrently making widespread public disclosure."[1] On October 22, 2019 at United European Gastroenterology Week (UEG) in Spain, a key annual GI conference, an ENIGMA trial investigator presented what we consider to be new, material, non-public information not disclosed in the August 5th topline results[2]. We found no disclosure of the event or slides on the ALLK site, prior to or since the event, nor any 8-K filing – unusual as companies with exciting results typically promote upcoming, marquee conference presentations. We note ALLK filed an 8-K for an almost identical presentation by a different investigator at ACG a week later, suggesting that the lack of disclosure was not accidental.

ENIGMA presentation at UEG, Oct 22, 2019



SEC action against pharma company in Aug 2019

SEC Signals New Phase of Regulation FD Enforcement

Tuesday, August 20, 2019

The **United States Securities and Exchange Commission** (SEC) announced today, August 20, 2019, that it **charged TherapeuticsMD, Inc., a pharmaceutical company headquartered in Boca Raton, Florida, with violations of Regulation FD** based on its disclosure of material, nonpublic information to sell-side research analysts.

Source: [1] https://media2.mofo.com/documents/faqs-regulation-fd.pdf; [2] http://www.professionalabstracts.com/ueg2019/iplanner/#/grid/1571702400; https://www.natlawreview.com/article/sec-signals-new-phase-regulation-fd-enforcement