Evaluate Vantage

December 22, 2020

# Source flop raises tezepelumab questions

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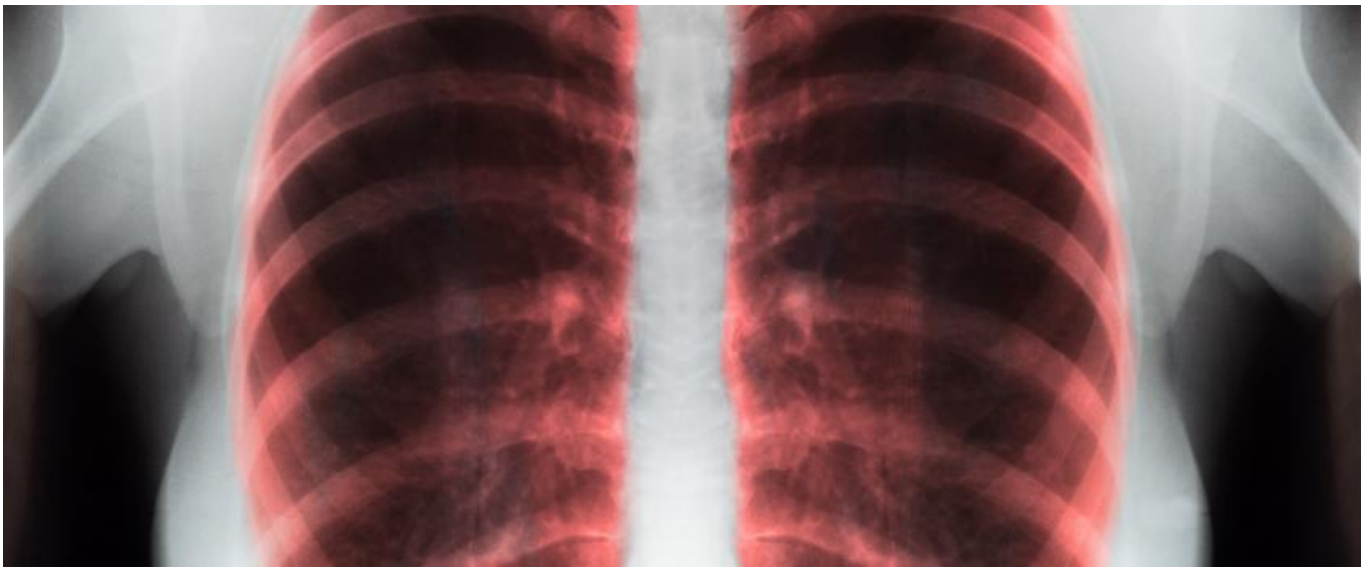

**Astrazeneca and Amgen hope the "totality of the data" will win out for their asthma project.**

Two out of three is not bad. But a pivotal failure for Astrazeneca and Amgen's big asthma hope tezepelumab, not long after a previous phase III success, raises questions about the project's approvability and eventual market.

Unfortunately there are not many answers yet: all the companies are saying is that the 150-patient Source study, in severe asthma patients receiving oral corticosteroids (OCSs), failed to hit its primary endpoint, reduction in daily OCS dose without loss of asthma control. Still, Astra remains confident of teze's chances, with a regulatory filing still slated for the first half of next year.

The companies noted that, on other efficacy measures, Source returned similar results to previous trials. Among other things, they might be referring to annualised asthma exacerbation rate, which is listed as the first secondary outcome measure in Source. This was also the primary endpoint of the larger phase III Navigator study, which was top-lined as a success in November (*Amgen finally Navigates a win, November 10, 2020*).

Full data from both Source and Navigator will be presented at an upcoming medical meeting, and it will be interesting to see whether the exacerbation data live up to those seen in the phase II Pathway trial, which found a 62-71% reduction versus placebo.

Also under scrutiny will be teze's performance in the tricky non-eosinophilic asthma population, for which there are few treatment options. Astra and Amgen have already said that Navigator hit in this subtype but investors will be keen to see the magnitude of effect here.

In Source, around a third of patients were classed as eosinophilic and around two thirds as non-eosinophilic. However, a spokesperson for Astra told *Evaluate Vantage* that the trial was too small to allow an analysis of the primary endpoint by subtype.

Another difference between Source and Navigator was that the latter required patients to have uncontrolled asthma, while the former did not.

**Design flaw?**

As for why Source failed, the companies said the trial's design might provide a potential explanation. An Astra spokesperson told *Evaluate Vantage* that Source had a longer duration than many other OCS-sparing trials of

asthma biologics, with an OCS-reduction phase of 36 weeks, versus 16-20 weeks for studies of Astra's Fasenra, Sanofi/Regeneron's Dupixent and Glaxosmithkline's Nucala.

The spokesperson added that, in Source, investigators could make an additional attempt to reduce the OCS dose even if the patient did not meet the OCS reduction criteria. Perhaps this led to a loss of asthma control in some patients, although more data will be needed to ascertain whether this is what scuppered the primary endpoint.

The Source failure is a particular blow to Amgen: teze is the group's biggest pipeline hope, with sellside consensus putting 2026 sales at $1bn, according to *EvaluatePharma*. The group's stock sank 2% this morning.

The companies believe the “totality of evidence”, including results from Navigator and Pathway, should support teze’s use in a broad severe asthma population. But the Source stumble has cast a dark cloud over the project’s previous success.