Evaluate Vantage

March 29, 2021

Humanigen claims a Covid-19 win with lenzilumab

Madeleine Armstrong

But the company focused on a modified intent-to-treat analysis of its pivotal trial.

So far, treatments for hospitalised patients with Covid-19 are few and far between. Humanigen believes that its anti-GM-CSF MAb lenzilumab could soon join these hallowed ranks, after reporting what it claimed were positive phase 3 results with the project today.

However, this success was based on a modified intent-to-treat analysis that excluded 33 patients – 19 in the active arm and 14 in the placebo cohort. As the study appears only to have narrowly met its primary endpoint in the mITT population, inclusion of these patients could have tipped the trial into failure.

Investors seemed untroubled, sending Humanigen's stock up 61% today.

Company execs said during a conference call today that the mITT analysis was the primary endpoint of the study, and added that mITT analyses were the standard across trials of Covid-19 agents, given the large number of patients who are typically randomised but do not end up receiving drugs.

However, a look at the Recovery trial, which was cited several times by the Humanigen execs, appears to contradict this view: cohorts of that study testing both dexamethasone and Roche's Actemra both used intent-to-treat analyses.

Enough for EUA?

Given the need for therapies to treat severe Covid-19 patients, Humanigen might still get its wish for an emergency use authorisation for lenzilumab based on this trial alone.

The study tested lenzilumab on top of standard of care in patients hospitalised for Covid-19 who had not yet progressed to mechanical ventilation. Around 88% of patients in the trial were receiving dexamethasone or other steroids, 62% were on Gilead's Veklury, and 57% were receiving both.

The primary endpoint was 28-day ventilator-free survival. In the mITT population, this was 16% for lenzilumab versus 22% for placebo, which Humanigen said showed a 54% increase in chances of staying ventilator-free across the 28 days. The resulting 0.0365 p value was statistically significant, it said, without disclosing its threshold for significance.

The company was asked during today's call to provide an analysis for the ITT population, but would not do so.

On mortality, Humanigen claimed a favourable "trend": The mITT analysis found that 10% of patients died in the lenzilumab arm versus 14% of those on placebo, with a non-significant p value of 0.2287. The company said the study was not powered to demonstrate a benefit here.

Lenzilumab is also being tested in the NIH-run Activ-5 study, but Humanigen hopes that the FDA will not need this for an EUA and, rather, that it could support a BLA planned towards the end of this year.

Success where Glaxo failed

Another question raised by today's data is why lenzilumab succeeded where Glaxosmithkline's anti-GM-CSF MAb otilimab failed (*Glaxo fails to win an Oscar, February 25, 2021*).

The answer might be the populations tested. Both trials enrolled hospitalised patients who needed oxygen support, but Glaxo's included patients on mechanical ventilation while Humanigen's did not.

Perhaps there is a window of opportunity for anti-GM-CSF MAbs in severe, but not too severe, Covid-19.

More answers could come soon. Glaxo has amended the protocol of its mid-stage study of otilimab, Oscar, to try to confirm a benefit seen in the over-70s. Meanwhile, mid-stage data are coming from two other anti-GM-CSF projects, from Kiniksa and I-Mab Biopharma.

Both trials have included patients on mechanical ventilation, but Kiniksa's is unique in looking at non-mechanically ventilated and mechanically ventilated groups separately.

Anti-GM-CSF antibodies in development for Covid-19		
Project	**Company**	**Status**
Lenzilumab	Humanigen	Ph3 trial positive Mar 2021
Otilimab	Glaxosmithkline	Failed ph2 Oscar trial, Glaxo amending protocol to explore benefit in over-70s
Mavrilimumab	Kiniksa	Data due from ph2 portion of ph2/3 in H1 2021
Plonmarlimab/TJ003234	I-Mab Biopharma	Interim analysis of p2/3 trial planned in Q2 2021
Source: EvaluatePharma & clinicaltrials.gov.		