Evaluate Vantage

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Regeneron joins Lilly in validating the Covid antibody approach

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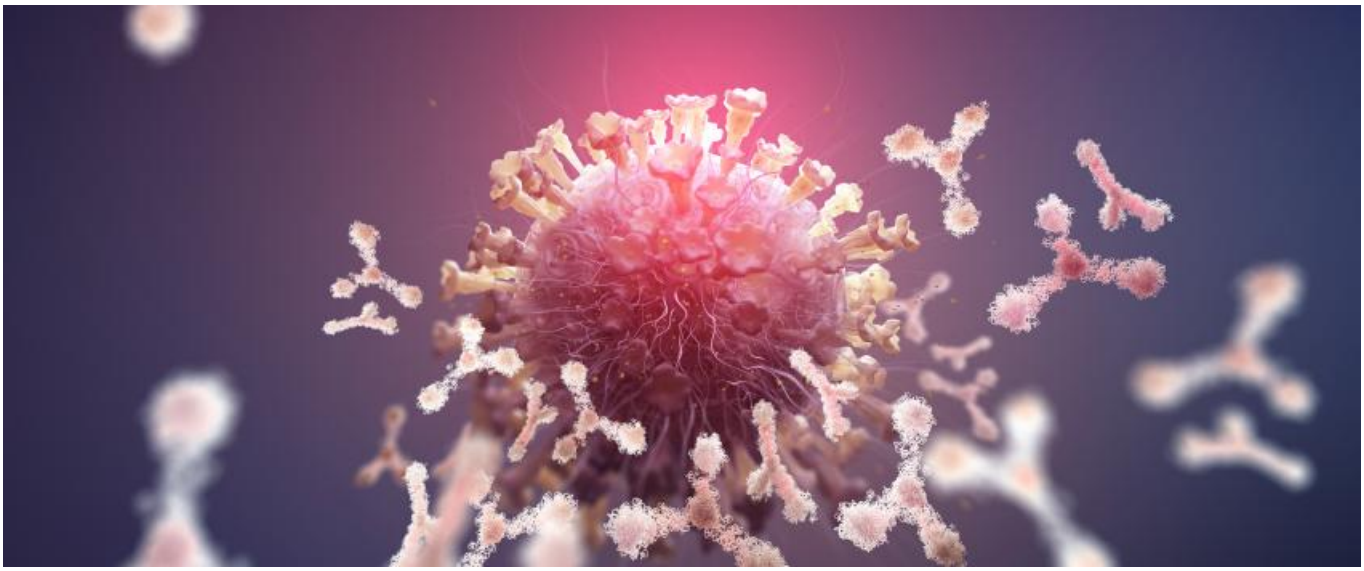


Like Lilly Regeneron reports promising but not emphatic data with its antibody treatment, and the question turns to approvability.

It is easy to find flaws in the first clinical results of Regeneron's anti-Covid-19 antibody cocktail, disclosed after market close yesterday, but in these pandemic times such detail is almost irrelevant.

What matters most is that the data validate the antibody approach, and a key question is whether they might also be enough to secure a US emergency use authorisation. Given that projects including convalescent plasma have received an EUA on much weaker data the answer might be yes, though Regeneron is for now keeping its options open.

On an analyst call last night the group said it had begun sharing the results with regulators, and that they would "be used to inform the next steps". Today its stock opened off 2%, so investors are unsure, but Evercore ISI analysts hinted at sales of $1bn a year as long as Covid-19 lingers, followed by the possibility of delivery to national stockpiles.

"Descriptive analysis"

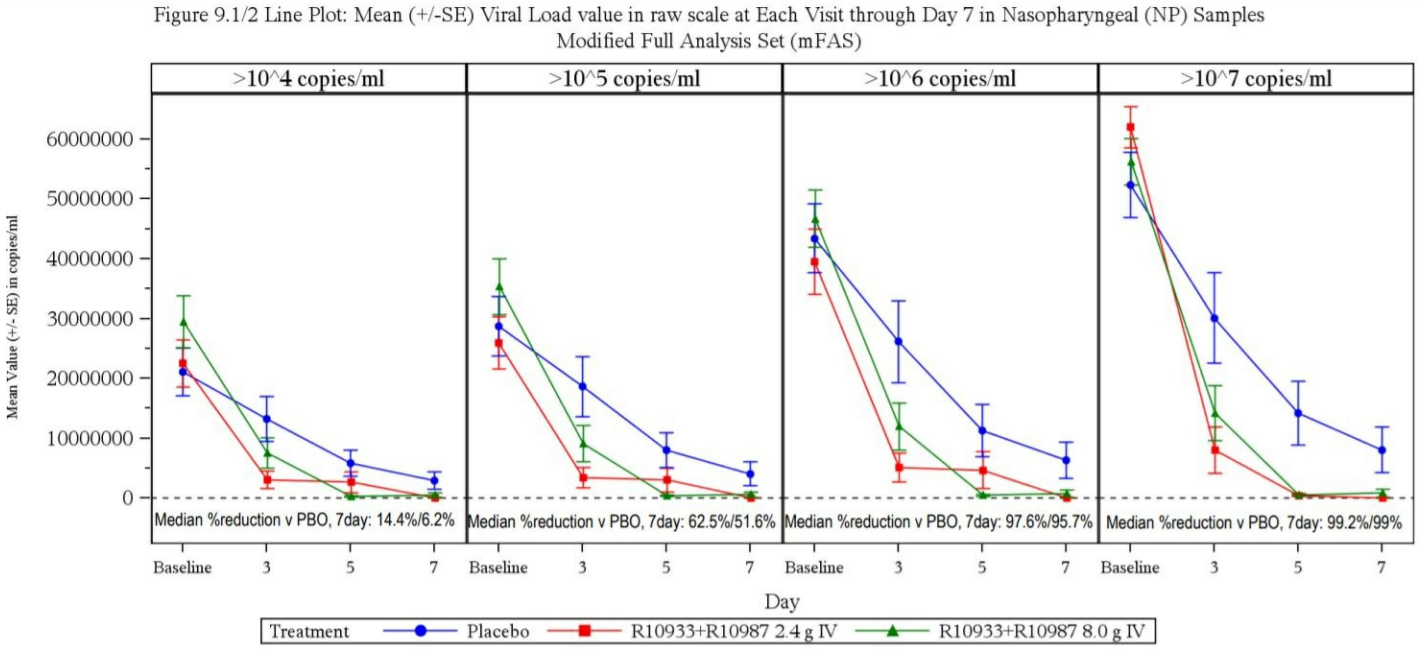
And this was just a snippet of the data Regeneron will hope to generate with the first of several trials of its cocktail of REGN10933 plus REGN10987.

What Regeneron curiously called a "descriptive analysis" came from a phase I/II/III trial in non-hospitalised patients with Covid-19. The data comprised only the first 275 patients enrolled, across two dose groups and placebo; the blinded study has a recruitment target of over 2,000.

Perhaps the most important finding was that Covid-19 viral loads were reduced most in patients with the highest load at baseline. A central part of Regeneron's thesis is that on infection some patients do not mount an effective immune response – these have very high viral loads – while those with low loads have already generated some antiviral antibodies.

Thus the company was emboldened to surmise that the patients in greatest need were the very ones who benefited most. It called this finding an "incredible correlation".

REGN-COV2 PROVIDED GREATER REDUCTION IN VIRAL LOAD IN THOSE WITH HIGHER VIRAL LOAD AT BASELINE



Source: Regeneron presentation.

The next question is how to identify patients with high viral load, which Regeneron called a major societal imperative. Regeneron is already partnered with one company working on a diagnostic for this purpose – Roche; one possibility is thus to use a diagnostic and therapeutic in concert.

What about the formal primary endpoints of Regeneron's trial? The study has five, three relating to safety, one concerning viral load reduction, and one regarding cutting Covid-19-related medical visits. Treatment-related adverse events and infusion-related and hypersensitivity reactions occurred rarely and fairly evenly across the three cohorts.

Though Regeneron highlighted the viral load reductions, even attributing p values below 0.05 to the high dose and to both doses combined in seronegative patients, it was careful not to call these statistically significant. With such small patient numbers this interim analysis must have had minimal alpha assigned to it, and Regeneron correctly called the p values nominal.

Confounding findings included the lack of a numerical dose-response relationship; according to Jefferies Regeneron is debating whether to continue only with the low dose. Also, the absolute viral load reductions look modest, though Evercore stressed that Covid-19 was an acute infection, so the drops seen could still be very meaningful clinically.

As for medical visits, there was a numerical reduction with the cocktail versus placebo, but with just 12 visits in total there is no way of discerning the relevance.

Targets

The two antibodies in Regeneron's cocktail hit different epitopes on the receptor-binding domain of Covid-19's Spike protein. Lilly is also targeting different Spike protein epitopes with two MAbs, LY-CoV555 and LY-CoV016, and has reported the first data with the former (*Lilly leads the Covid antibody charge, September 16, 2020*).

Overall the same can be said of both datasets: the findings are promising, but by no means emphatic. They should help shift some of the spotlight from vaccines to treatments, though of course both are necessary to combat the pandemic.

Vaccine developments are themselves proceeding apace, with Curevac today starting phase II trials of CVnCoV and Moderna having data from a trial of mRNA-1273 in old adults published in the NEJM. Meanwhile, Inovio's controversial project, INO-4800, was on Monday put on US clinical hold.

The next data point to watch from Regeneron will be a study in hospitalised patients, and here already the signs are good: the group says these patients tend to have much higher viral loads than ambulatory subjects. Of course, if an EUA is granted soon this might become academic.

Selected trials of Regeneron's MAb cocktail REGN-COV2 (REGN10933 + REGN10987)			
Study	**Trial**	**Recruitment target**	**Data?**
Ph1/2/3, ambulatory patients	Study 2067	2,104 (symptomatic & asymptomatic)	"Descriptive analysis" released on first 275 symptomatics
Ph1/2/3, hospitalised patients	Study 2066	2,970 (4 cohorts depending on oxygen requirement)	Jan 2021 primary completion
Ph3 prevention	Study 2069	2,000 (SC dosed household contacts study)	Jun 2021 primary completion
Ph3, hospitalised patients	Recovery	15,000 (IV dosed UK NHS study)	Dec 2021 primary completion
Source: Regeneron & clinicaltrials.gov.			