

The wait for AstraZeneca's pivotal Covid-19 vaccine data



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As the frontrunners in the Covid-19 vaccine race pull ahead Astra touts promising immunogenicity data in older adults.

New phase II immunogenicity data with AstraZeneca's Covid-19 vaccine candidate AZD1222 suggest that the project might work as well in older adults as it does in younger people. But these are not the data that investors are looking for; efficacy results from Astra's phase III trials in the UK and Brazil have not yet emerged, despite hopes among some analysts that these might be reported in mid-November.

While Astra's chief financial officer told an investor meeting this week that the phase III results were "imminent", there were hints this morning from Astra's partner, the University of Oxford, that readout from the UK study had been delayed by falling numbers of Covid-19 cases over the summer.

The data before Christmas?

Some analysts, [including Jefferies](#), had hoped to see pivotal data by mid-November, basing their assumptions around infection rates and the UK study's statistical analysis plans.

But the official line from Astra has long been that data are coming by the end of the year. Astra's chief executive, Pascal Soriot, downplayed expectations of a November readout during the group's third-quarter earnings call on November 5.

And in an interview with UK BBC Radio 4 today, Professor Andrew Pollard, head of the Oxford Vaccine Group and an investigator in the UK phase II/III COV002 trial, struck a cautious tone. While he said the unblinding of that study would "definitely" take place before Christmas, he added: "We're not quite there because of the great success we've had controlling the pandemic over the summer months."

This meant "very few cases" of Covid-19 in the trial, which "really slowed things down", he said. However, the situation has changed in the past month or so, with cases on the rise again in the UK. Professor Pollard said this made him more confident of getting the data soon.

In an unfortunate twist for Astra, readout of its rivals' pivotal Covid-19 vaccine trials had been hastened by surging cases in the US.

And in the US Astra has fallen even further behind after an adverse event, thought to be transverse myelitis, forced it to [put its phase III trial there on hold](#). This study was restarted in late October; it was quietly slipped

out in Astra's [third-quarter results presentation](#) that its recruitment target had been increased from 30,000 to just over 40,000.

The delay to the US study has made the UK trial even more important. According to the [latest trial protocol for the latter](#), the primary evidence of AZD1222's efficacy will come from a pooled analysis of phase I/II studies in the UK and South Africa, the UK phase II/III study, and a phase III trial in Brazil.

However, it is unclear whether the FDA will allow these results to support a filing without at least some US data available – particularly after the recent strong efficacy results with Pfizer/Biontech's BNT162b2 and Moderna's mRNA-1273.

Selected trials of AZD1222				
Country	Phase	N	Trial name	Trial ID
UK	Ph1/2	1,090	COV001	NCT04324606
UK	Ph2/3	12,390	COV002	NCT04400838
Brazil	Ph3	10,000*	COV003	NCT04536051
South Africa	Ph1/2	2,000	COV005	NCT04444674
US	Ph3	40,051*	-	NCT04516746

**Increase in trial size disclosed during Astra's third-quarter 2020 results.
Source: EvaluatePharma, clinicaltrials.gov.*

Still, Professor Pollard maintained that multiple vaccines would be needed to defeat Covid-19. One unique selling point for AZD1222 is its storage requirements; BNT162b2 and mRNA-1273 must be shipped at -70°C and -20°C respectively, which could cause distribution headaches particularly in lower-income nations, while Astra's vaccine can be stored in the fridge for up to a year.

And now the UK company also has immunogenicity data suggesting a similar immune response in older people and younger adults. It was once feared that older people would fail to respond to Covid-19 vaccines – a concern as immune response declines with age – but these worries now seem to have been assuaged.

The results, [published in The Lancet today](#), found comparable levels of neutralising antibodies in people receiving two doses of the vaccine across the three age groups studied: 18-55, 56-69, and 70 or over. T-cell responses were also similar.

Good as they are, these data will probably not give Astra an edge over the frontrunners. mRNA-1273 has [already shown similar immune responses in younger and older adults](#); BNT162b2's [immunogenicity data in the older population were not as strong](#), but the final phase III results, reported yesterday, [found 94% efficacy in people aged over 65](#).

And Astra still has to prove that these antibody responses translate into efficacy in preventing Covid-19. The world is now waiting for its phase III data.