

Covid-19 vaccines remain hot - in spite of Inovio



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Biontech and Pfizer come roaring back with the first human data on BNT162, a day after Inovio's effort disappointed.

Inovio's attempt yesterday to generate interest in a very limited clinical dataset on its Covid-19 vaccine fell flat, sending the pandemic-focused biotech's stock down 15%. But competing approaches could do better, and investors are keenly awaiting imminent readouts from several other vaccine players.

Just today, for instance, the first human data were revealed for Biontech/Pfizer's BNT162b1, in a non-peer reviewed preprint, showing strong neutralising antibody levels being elicited in all 36 subjects dosed. This project is a shot across the bows at Moderna, which in May was first to [dribble out case reports on a Covid-19 vaccine given to humans](#).

Like Moderna's mRNA-1273, BNT162b1 is an mRNA vaccine - a novel approach also used in a separate [Sanofi/Translate Bio project that saw a \\$425m fee handed across last month](#). The Biontech/Pfizer BNT162 project actually [comprises four different approaches](#), and the b1 iteration is nanoparticle-formulated and nucleoside-modified; it encodes the Covid-19 spike glycoprotein.

The highlight of today's [scientific paper preprint](#) is data on neutralising antibodies - the really important ones, which interfere with a virus's ability to infect a cell.

36 subjects given single doses of 10µg, 30µg or 100µg showed neutralising antibody levels of between 0.9x and nearly twice those seen in a panel of sera from recovered subjects, within 21 days. The two low doses were given a second time, and within seven days the levels clocked in at 8x to 46x those in the convalescent sera.

Of course, it is not clear whether this will be enough actually to protect from serious infection, but the result is strongly encouraging. On the safety side, fatigue and headache were more common with BNT162b1 than control (an additional nine subjects got placebo), but there were two severe adverse events: grade 3 pyrexia and sleep disturbance.

Inovio's (and Moderna's) loss

Pfizer and Biontech both traded up this morning, 4% and 5% respectively. Meanwhile, Moderna was off 7%, while Inovio lost another 17%, one day after slumping 15%.

It was Moderna that in May said 45 volunteers given mRNA-1273 were producing binding antibodies, though data on neutralising antibodies were only available from eight subjects, all of whom were said to be producing

these too.

Clearly the markets have rewarded Pfizer and Biontech for a more complete dataset. Moderna might not recover until its next catalyst, publication of the mRNA-1273 clinical data in a peer-reviewed journal, which should help investors decide whether the effect is real or if the company was just cherrypicking data.

The situation is much worse for Inovio, a biotech famous for jumping on pandemic bandwagons – from bird flu to swine flu to Ebola, Zika, Mers and finally Covid-19 – without yet bringing a single vaccine to market.

Inovio said yesterday that 34 of 36 volunteers in its phase I trial demonstrated “overall immune responses” six weeks after receiving two doses of INO-4800. What this actually meant was not immediately clear, and little else was disclosed; importantly, the company failed to say how many patients produced neutralising antibodies against the coronavirus.

Earlier, [a paper published in The Lancet](#) on Cansino’s adenovirus vaccine Ad5-nCoV also disappointed. 108 volunteers were given one of three doses, but only 50-75% of the subjects developed levels of neutralising antibodies that were deemed to be sufficiently high.

Selected vaccines in development for Covid-19			
Company/org	Vaccine	Type	Detail
Moderna/NIAID	mRNA-1273	mRNA vaccine	8/8 volunteers producing strong neutralising antibody levels; data on remaining 37 not made available
Cansino Biologics	Ad5-nCoV	Adenovirus type 5 vaccine	50-75% of 108 volunteers generating neutralising antibodies
Inovio	INO-4800	DNA vaccine	Immune responses claimed, but no data on neutralising antibodies
Biontech/Pfizer	BNT162b1	mRNA (modRNA) vaccine	36/36 volunteers producing strong neutralising antibody levels
Biontech/Pfizer	BNT162a1, BNT162b2 & BNT162c2	mRNA (uRNA, modRNA & saRNA) vaccines	Phase 1 data due Jul 2020
Astrazeneca/ Uni of Oxford	AZD1222	Chimp adenovirus vaccine	Phase 1 data due Jul 2020
Novavax	NVX-CoV2373	Nanoparticle vaccine	Phase 1 data due Jul 2020
Dynavax/Clover/GSK	COVID-19 S-Trimer	Trimerised fusion protein	Phase 1 data possible Aug 2020
Johnson & Johnson	?	Adenovirus type 26 vaccine	Phase 1 starting Jul 2020
Translate Bio/Sanofi	?	mRNA vaccine	Phase 1 starting Q4 2020

Source: WHO list, EvaluatePharma & company statements.

This is not the end of the race, and investors have plenty more data to look forward to on Covid-19 vaccines. For one thing, the three other iterations of BNT162 should generate phase I results imminently, as should AZD1222, a more traditional, viral vector-based vaccine being developed by [Astrazeneca in a 1,000-patient trial in collaboration with the University of Oxford](#).

So, when clinical data come out, what should investors be looking for?

Levels of neutralising antibodies – at least up to a target level, with the general rule that the higher the better – are essential. So is safety, given that a Covid-19 vaccine would be expected to be given to a broad patient population, and investors should look for an absence of inflammatory symptoms and should examine disclosed adverse events closely.

In addition to humoral (antibody-based) immunity it might also be important to show that a vaccine is eliciting T-cell responses; both might be necessary to prevent a severe Covid-19 infection.

There is still much to play for, especially given the scope for accelerated development, and a view that countries might not exit fully from lockdown until a Covid-19 vaccine is available. That said, the early winners and losers have now emerged.

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