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# Covid-19 vaccine contest turns to T-cell responses

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**The coronavirus vaccine race now features three front runners with clinical data, and at least one boasts impressive T-cell responses.**

In the race to develop a vaccine against Covid-19 Moderna and Biontech/Pfizer's rival projects have shown an impressive ability to generate neutralising antibodies, but so far little had been said about their ability to stimulate T-cells. Today that changed.

Not only did Astrazeneca's AZD1222 join the leaders with the first clinical data of its own published in the *Lancet*, these included findings on its ability to generate a T-cell response. But it was Biontech/Pfizer that, in a preprint of a separate trial of their BNT162b1 vaccine, detailed perhaps the most impressive T-cell responses so far.

It has been hypothesised that to prevent severe Covid-19 infection and generate a long-lasting effect it might be necessary for a vaccine to stimulate cellular as well as humoural (antibody-based) immunity. Both are key parts of an immune response that ultimately leads to the destruction of a pathogen.

**Antibodies... and more**

Astrazeneca today reported data on just part of the patient population it wants to enrol. The Astra/Oxford University trial has so far enrolled 1,077 subjects, but the Lancet paper's key findings relate to 35 for whom neutralising antibody levels are available.

91% showed detectable neutralising antibody responses after a single AZD1222 dose, and this became 100% after a booster, the authors wrote. Neutralising antibodies are key as they interfere with a virus's ability to infect a cell.

T-cell response data, meanwhile, were available for 43 subjects, and a response was induced in all, "peaking by day 14, and maintained two months after injection", Astra said in a statement. However, the Lancet paper was low on detail, and revealed that "a boost in cellular responses was not observed following the second dose".

Moreover, nothing was said about whether these were CD4+ (helper) or CD8+ (killer) T-cell responses. This could disappoint investors who had been enthused by a UK press report on Friday that stressed stimulation of killer T cells.

| Cross-trial comparison of Biontech/Pfizer, Moderna and Astrazeneca data | | | |
|---|---|---|---|
| **Project (company)** | **Study** | **Neutralising antibodies** | **T cells** |
| BNT162b1 (Biontech/Pfizer) | NCT04368728 | 36/36 volunteers producing strong levels | No data |
| BNT162b1 (Biontech/Pfizer) | NCT04380701 | 48/48 volunteers producing strong levels | RBD-specific CD8+ responses, up to 0.4% of cells in 29/36 |
| | | | |
| mRNA-1273 (Moderna) | NCT04283461 | 45/45 volunteers producing strong levels | S-specific CD8+ responses, up to 0.2% of cells |
| | | | |
| AZD1222 (Astrazeneca) | NCT04324606 | 32/35 volunteers producing strong levels, rising to 35/35 after booster | Unspecified T-cell responses, up to 0.7% of cells in 43/43 |
| *Source: scientific paper preprints, NEJM & Lancet. RBD=receptor-binding domain.* | | | |

For its part, Biontech/Pfizer pre-empted the Lancet publication with publication of another scientific paper pre-print, this time relating to a German trial of the mRNA vaccine project BNT162b1, and specifically highlighting its effect on CD8+ T cells.

The trial enrolled 60 subjects across four 1-50µg dose levels. 36 of these were tested for a cellular response, the companies said, and 29 mounted what it called a functional CD8+ T-cell response "comparable to memory responses observed against CMV, EBV and influenza virus".

What is more, these cellular responses were against the Covid-19 receptor-binding domain, implying a very precise response against the antigen that BNT162b1 encodes. There was no dose-response relationship, which the authors argued was positive, implying that responses could be mounted with even a low dose.

Moderna's mRNA rival mRNA-1273 had shown effects on T cells when its study was published in the *NEJM* last week, but these were seen as being somewhat modest. mRNA-1273 encodes not the binding domain but the entire spike (or S) protein, and the responses were said to be S-specific.

The first BNT162b1 study reported, a US trial in 36 evaluable volunteers, had shown strong neutralising antibody responses, but nothing was said about T cells (*Covid-19 vaccines remain hot – in spite of Inovio, July 1, 2020*).

No doubt investors will continue to pick apart all these data over the coming days. But the Covid-19 tectonic plates have shifted again: Biontech this morning rose 5%, while Astra was unmoved and Moderna lost 10%.