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AACR 2022 – Biontech’s cell therapy effort bears fruit at last

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But it’s still far too early to tell whether combining Car-T with an mRNA vaccine might improve response durability.

Having taken years to get its first Car-T project, BNT211, into the clinic Biontech appears to be making some progress at last. Data from its first-in-human solid tumour study, presented at AACR today, have shown six responses among 14 efficacy-evaluable subjects.

The trial will be of interest for another reason too: it is the first human test of Biontech’s move to improve the expansion and persistence of Car-T cells by following their infusion with doses of an antigen-encoding nanoparticulate mRNA vaccine. Still, based on the early data there is no way yet of telling whether the combo boosts either initial or long-term efficacy.

Presenting the results at a clinical trials plenary Dr John Haanen, of the Netherlands Cancer Institute, cautioned against drawing major conclusions from the data, which were very early and comprised few patients. Five of the six responding subjects have shown improving cancer shrinkage, but this includes BNT211 monotherapy as well as the mRNA vaccine combo cohorts.

Compelling

Nevertheless, there has been excitement about the approach. Berenberg analysts, for instance, have called the scientific rationale behind Biontech’s work “compelling”, while cautioning that there are questions about the durability and impact of mRNA drugs on Car-T cells.

BNT211 targets Claudin-6, an antigen said to be expressed on solid tumours. The mRNA vaccine, which Biontech calls CARVac, itself encodes Claudin-6, promoting its expression on dendritic cells, and preclinical work has suggested that this works to stimulate the BNT211 cells to a greater extent than the endogenous antigen on its own.

At last year’s Esmo-IO meeting Biontech had provided the first glimmers of BNT211’s efficacy in a phase 1 study, which at the time comprised eight evaluable monotherapy subjects, and two in a combo cohort in which CARVac was administered every two or three weeks up to 100 days after the BNT211 transfer.

There were two partial remissions in each cohort. At AACR, with four more patients evaluable, two additional partial remissions have been seen, and one of the earlier partial responses has deepened to a complete one, continuing six months post-infusion.

Claudin-6 expression

Though on the face of it the ORR stands at 43% two further combo patients were dosed but discontinued before reaching efficacy evaluation at six weeks, so they do not appear in the denominator. The trial encompasses relapsed solid tumours, but these must be shown to be expressing Claudin-6; the responses seen comprise four testicular and two ovarian cancer patients.

As ever with cell therapies safety will remain closely watched. Across the 16 study subjects there were 37 treatment-related adverse events graded severe, including two dose-limiting toxicities, a grade 4 cytopenia and grade 4 haemophagocytic lymphohistiocytosis; but cytokine release was said to be manageable, and there was no neurotoxicity.

BNT211 had appeared as a preclinical project in Biontech's pipeline years before the company became a force in Covid vaccines, and a clinical trial had initially been planned for 2016. But it was only in 2020 that the phase 1 study got under way; two years on, and the company at least has a reason to press on.