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BNT211: A PHASE I/II TRIAL TO EVALUATE SAFETY AND EFFICACY OF CLDN6 CAR-T CELLS AND VACCINE-MEDIATED IN VIVO EXPANSION IN PATIENTS WITH CLDN6-POSITIVE ADVANCED SOLID TUMORS

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Background BNT211 is a chimeric antigen receptor (CAR)-T cell product candidate that targets the tumor specific antigen Claudin-6 (CLDN6). Preclinical studies demonstrated that combining these engineered cells with a CAR-T cell Amplifying RNA Vaccine (CARVac) leads to in vivo expansion of adoptively transferred CAR-T cells, resulting in their improved persistence and functionality.

Methods This first-in-human, open label, multi-center trial involves a bifurcated 3+3 design with separate CLDN6 CAR-T cell dose escalations (single flat-dose) for monotherapy (part 1) and the combination with CARVac (part 2) based on 3 dose levels (DL). In part 2, CARVac is applied every 3 weeks starting at day 4 post transplantation including a one-step intra-patient dose escalation. Patients with CLDN6-positive relapsed or refractory solid tumors without further standard treatment options and ECOG 0 or 1 are eligible for recruitment.

Results As of July 23rd 2021, 8 patients have been treated. DL1 of part 1 has been completed, while dosing of part 1 DL2 and part 2 DL1 is ongoing. One patient with cancer of unknown primary was treated with a dose below DL1 in combination with CARVac; the underlying diseases of the other 7 treated patients were testicular, ovarian and endometrial cancer as well as soft-tissue sarcoma. No acute or dose-limiting toxicities and no serious adverse events related to the drug product have been reported. Manageable cytokine release syndrome (CRS, grade 1-2, the latter managed with Tocilizumab) without any signs of neurotoxicity have been observed in both patients of part 1 DL2. Only transient and moderate elevations of IL-6 and CRP serum levels occurred in remaining patients. Notably, administration of CARVac resulted in transient flu-like symptoms resolving within 24h. Analysis of CAR-T cell frequency in peripheral blood revealed robust engraftment followed by decline after day 17. Further expansion was noted in two patients with liver metastases accompanied by elevated levels of ALT, AST and AP, while total bilirubin was not affected. First tumor assessment 6 weeks after transplantation available for 5/8 patients revealed 4 SD (3 transitioned into PD after an additional 6-18 weeks) and 1 PD. Strikingly, three patients showed initial tumor shrinkage according to RECIST1.1 (reduction of target sum: -18%, -21% and -27%).

Conclusions CLDN6 CAR-T cells +/- CARVac show a favorable safety profile at doses tested and encouraging signs of efficacy. Updated data from open cohorts and especially for combination with CARVac will be presented.

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Trial Registration ClinicalTrials.gov: NCT04503278

REFERENCES

N/A

Ethics Approval Ethics & Institutional Review Board approvals were obtained from the respective participating countries prior to initiation of the trial.

Consent N/A

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