PRELIMINARY SAFETY, PK/PD AND EFFICACY RESULTS FROM A FIRST-IN-HUMAN PHASE I/IIA CLINICAL TRIAL OF BNT411, A SYSTEMIC TOLL-LIKE RECEPTOR 7 AGONIST IN PATIENTS WITH SOLID TUMORS

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Background The intravenously administered small-molecule Toll-like receptor 7 (TLR7) agonist BNT411 was developed to systemically activate plasmacytoid dendritic cells, characterized by a Type 1 interferon-dominated release of cytokines. The activation of cytotoxic CD8+ T cells and broad modulation of the innate immune system is intended to enhance pre-existing anti-tumor responses and induce de novo responses, especially in combination with cytotoxic therapies and immune checkpoint inhibitors.

Methods This first-in-human, open label, multi-center trial (BNT411-01) involves dose titration in patients (ECOG 0 or 1) with solid tumors with BNT411 administered weekly (q1w) for a month, then q3w thereafter until disease progression, unacceptable toxicity, or death. Part 1A is a single-agent dose escalation (accelerated titration) of BNT411 in patients with metastatic or unresectable solid tumors that have exhausted available treatment options, with bifurcation to Part 1B, a dose escalation of BNT411 in combination with atezolizumab, carboplatin and etoposide in patients with chemotherapy-naïve extensive-stage small cell lung cancer (ES-SCLC), followed by expansion cohorts (Part 2). Endpoints of Part 1A and 1B are safety, determination of maximum-tolerated dose (MTD)/recommended phase 2 dose (RP2D), pharmacokinetics, pharmacodynamic (PD) profiling of immune activation, and preliminary efficacy of BNT411 (RECIST 1.1).

Results As of 1st July 2021, 11 patients have received BNT411 in Part 1A and 5 of 8 dose levels have been cleared. Patients (median age 62 years) had previously received a median of 3 (range 2–5) prior systemic cancer therapies. The only drug-related adverse events (AEs) reported in two or more patients were pyrexia (n=2 patients [18.2%], Grades 1 and 3 [non-serious]) and anaemia (n=2 patients, [18.2%], Grades 1 and 2). There were no dose limiting toxicities, grade 4–5 AEs, or related SAEs reported. Plasma cytokine levels showed the strongest response at BNT411 Dose Level (DL) 5 (2.4 µg/kg), with an increase (2.7–9.2 fold) of interferon-γ induced protein IP10 in 3/4 patients. The best response seen was 5 months of stable disease in one patient with squamous cell carcinoma of the lung at DL4 after 13 doses. Three dose levels remain to be tested in Part 1A (up to 16 µg/kg), with recruitment to Part 1B initiated.

Conclusions BNT411 has an acceptable safety profile at all doses tested as monotherapy, with encouraging PD signals that warrants study continuation. Updated data will be presented, including combination treatment in the first-line setting of ES-SCLC.

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Trial Registration ClinicalTrials.gov: NCT04101357

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

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