421 **A FIRST-IN-HUMAN (FIH) PHASE I/IIA CLINICAL TRIAL ASSESSING A RIBONUCLEIC ACID LIPOPLEX (RNA-LPX) ENCODING SHARED TUMOR ANTIGENS FOR IMMUNOTHERAPY OF PROSTATE CANCER; PRELIMINARY ANALYSIS OF PRO-MERIT**

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Background PRO-MERIT is a FIH, open-label, multicenter, Phase I/IIa trial investigating a liposomal RNA vaccine (BNT112) targeting the prostate cancer tumor-associated antigens (TAAs) kallikrein-2, kallikrein-3, acid phosphatase prostate, homeobox B13 (HOXB13), and NK3 homeobox 1. BNT112 is being investigated as monotherapy and in combination with cemiplimab in patients with metastatic castration-resistant prostate cancer (mCRPC) and newly diagnosed high risk localized prostate cancer (LPC).

Methods The trial involves dose titration in mCRPC patients (who have progressed after at least 2 but no more than 3 lines of systemic therapy) with BNT112 monotherapy (Part 1, fully recruited), followed by expansion cohorts (Part 2, recruiting) in both mCPRC and LPC with either BNT112 as monotherapy or in combination with cemiplimab. Primary trial endpoints investigate safety, tolerability, and preliminary anti-tumor activity (by Prostate Cancer Working Group 3 criteria). Secondary endpoints include determination of systemic induction or expansion of vaccine antigen-specific T cells. Vaccine-induced immune responses are analyzed *ex vivo* using an interferon-γ enzyme-linked immune absorbent spot (ELISpot) assay and following short-term *in vitro* stimulation.

Results As of 17 May 2021, 11 patients have received BNT112 monotherapy (9 Part 1; 2 in Part 2) and 3 patients have received BNT112 in combination with cemiplimab (at least one cycle completed). In Part 1, all 9 patients were stage IV at diagnosis and were receiving androgen deprivation therapy. Median age was 68 years. Two out of 9 patients experienced Grade 3 hypertension, leading to one dose reduction, that was initially reported as dose-limiting toxicity (DLT). All recovered within 24 h with no sequelae and the Safety Review Committee eventually concluded the events did not meet the DLT definition. Most common related adverse events (AEs) were pyrexia and hypertension. Eight serious AEs were reported in 5 patients, all unrelated to BNT112. In the 5 patients in Part 2, no additional safety signals or concerns were identified to date, either with BNT112 as monotherapy or in combination with cemiplimab. ELISpot data showed vaccine-induced immune responses were present in 7/7 ELISpot-evaluable patients. All 5 BNT112 TAAs were found to be immunogenic. Responses to each antigen were observed in at least 2 subjects. Initial responses with decreased prostate-specific antigen (PSA) levels have been observed in 2 patients in the BNT112 monotherapy arm.

Conclusions These data suggest that BNT112 has an acceptable safety profile. Additionally, BNT112 induces robust immune and PSA responses in patients with advanced prostate cancer.

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Trial Registration ClinicalTrials.gov: NCT04382898.

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

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