AN RNA-LIPOPLEX (RNA-LPX) VACCINE DEMONSTRATES STRONG IMMUNOGENICITY AND PROMISING CLINICAL ACTIVITY IN A PHASE I TRIAL IN CUTANEOUS MELANOMA PATIENTS WITH NO EVIDENCE OF DISEASE AT TRIAL INCLUSION

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Background Lipo-MERIT is an ongoing, first-in-human, open-label, dose-escalation Phase I trial investigating safety, tolerability and immunogenicity of BNT111 in patients with advanced melanoma. BNT111 is an RNA-LPX vaccine targeting the melanoma tumor-associated antigens (TAAs) New York esophageal squamous cell carcinoma 1 (NY-ESO-1), tyrosinase, melanoma-associated antigen 3 (MAGE-A3), and transmembrane phosphatase with tensin homology (TPTE). A previous exploratory interim analysis showed that BNT111, alone or combined with immune checkpoint inhibition (CPI), has a favorable adverse event (AE) profile, gives rise to antigen-specific T-cell responses and induces durable objective responses in CPI-experienced patients with unresectable melanoma.¹ Here, we present preliminary data in patients with no evidence of disease (NED) at trial inclusion in the BNT111 monotherapy subgroup.

Methods Patients with stage IIIB/C and IV pre-treated cutaneous melanoma were intravenously administered with BNT111 using a prime/repeat boost protocol. Patients were treated in seven dose escalation cohorts (7.2 to 400 µg total RNA) and three expansion cohorts to further explore dose levels of 14.4, 50 and 100 µg. In this analysis, patients receiving BNT111 monotherapy were grouped as having evidence of disease (ED) or NED, and immunogenicity, efficacy and safety were evaluated. Vaccine-induced immune responses were analyzed using an interferon-γ enzyme-linked immune absorbent spot (ELISpot) assay directly *ex vivo*.

Results As of May 24, 2021, 115 patients have received BNT111 within the Lipo MERIT trial. Of 71 patients treated with BNT111 monotherapy, 38 patients had ED and 33 patients had NED after prior therapies. Baseline characteristics were similar between the two groups. ELISpot data revealed comparable BNT111-induced T-cell responses against at least one TAA in ED vs. NED patients (14/22 [64%] and 19/28 [68%] patients with available ELISpot-evaluable samples, respectively), suggesting that BNT111 has the ability to induce T-cell immunity irrespective of the presence of a detectable tumor. As previously reported for ED patients, vaccine-induced CD4⁺ as well as CD8⁺ T-cell responses were also observed in NED patients, with a substantial fraction of *de novo* induced responses undetectable prior to vaccination. In NED patients, clinical efficacy was promising; median disease-free survival was 34.8 months (95% confidence interval: 7.0–not reached). The safety profile was similar in ED vs. NED patients; 38/38 (100%) and 32/33 (97%) patients experienced related treatment-emergent AEs, respectively, of which the majority were mild-to-moderate flu-like symptoms.

Conclusions Immunogenicity and safety profiles of BNT111 monotherapy were comparable in ED and NED patients. Promising signs of clinical activity were observed in NED patients.

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Trial Registration ClinicalTrials.gov: NCT02410733; EudraCT No. 2013-001646-33.

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Ethics Approval Ethics & Institutional Review Board approval was obtained prior to initiation of the trial (2018-13393_21-AMG federführend).

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