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Primary results from a randomized phase II trial of BNT111 in combination with cemiplimab with calibrator monotherapy arms in anti-PD-(L)1 relapsed/refractory melanoma

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Background

BNT111 is an investigational uridine RNA-based lipoplex cancer immunotherapy targeting the non-mutated, tumor-associated antigens NY-ESO-1, MAGE-A3, Tyrosinase and TPTE. A previous phase 1 trial (Lipo-MERIT) established a tolerable dose range and indicated early signs of clinical activity of BNT111 monotherapy (mono) and in combination with PD-1 inhibition in heavily pre-treated melanoma. Here, we present data from the phase 2 BNT111-01 trial in patients (pts) with unresectable Stage III or IV non-acral cutaneous melanoma (NACM).

Methods

The open label, randomized, multi-site, interventional phase 2 BNT111-01 trial (NCT: 04526899) aims to determine efficacy of BNT111 + cemiplimab (cemi) in anti-PD-(L)1 refractory/relapsed pts with NACM. Pts were randomized 2:1:1 to Arm 1 (BNT111 + cemi) and calibrator arms 2 (BNT111 mono) and 3 (cemi mono). The primary endpoint is objective response rate (ORR) by blinded independent central review according to RECIST 1.1 in Arm 1 vs a hypothetical historical control of 10% (H0-hypothesis). Secondary endpoints include safety, progression-free survival (PFS) and overall survival (OS).

Results

184 pts were randomized (94 in Arm 1, 46 in Arm 2, 44 in Arm 3), with comparable baseline characteristics between arms (median age 64.5 years; range 18 – 91). As of 14 FEB 2025, median follow-up was 15.6 months (mo). ORR of BNT111 + cemi was 18.1%, including 11 complete and 6 partial responses, resulting in rejection of the H0 hypothesis. Disease control rate (DCR) was 55.3%, median duration of response was not reached, median PFS was 3.1 mo and median OS 20.7 mo. ORR, DCR, median PFS and median OS for BNT111 mono were 17.4%, 58.7%, 2.8 mo and 13.7 mo; for cemi mono they were 13.6%, 47.7%, 3.2 mo and 22.3 mo, respectively. The safety profile in 181 treated pts was manageable, with typical cytokine release-related treatment-emergent adverse events in BNT111 treatment arms.

Conclusions

BNT111 + cemi in advanced NACM indicated statistically significant improvement against an assumed historic control ORR of 10%. BNT111 also indicated clinical activity as monotherapy. No meaningful differences in median PFS or OS were noted between combination and monotherapies.

Clinical trial identification

NCT04526899, EudraCT 2023-509513-36-00.

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BioNTech SE.

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Disclosure

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