TPS8129 **Poster Session**

A global phase III, double-blind, randomized trial of BNT327/PM8002 plus chemotherapy (chemo) compared to atezolizumab plus chemo in patients (pts) with first-line (1L) extensive-stage small cell lung cancer (ES-SCLC).

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Background: SCLC is an aggressive form of lung cancer. Incorporating immunotherapy for ES-SCLC pts in the frontline has improved outcomes, but long-term benefit is still lacking. There is an urgent need for efficacious treatments that can extend the duration of response and improve survival in SCLC. BNT327 is an investigational bispecific antibody, targeting both PD-L1 and VEGF-A in the tumor and tumor microenvironment (TME). By binding to PD-L1 on tumor cells it is designed to restore effector T-cell function and by binding to VEGF-A within the TME it also reverses the negative impact of VEGF signaling on immune cell infiltration and activation. In addition, via VEGF-A neutralization, it normalizes tumor vasculature. This dual targeting of PD-L1 and VEGF-A aims to deliver better efficacy and safety. Preliminary results from a Phase II trial showed encouraging efficacy results and a manageable safety profile for BNT327 with paclitaxel as second-line (2L) treatment of pts with SCLC (1992P, ESMO 2023). Combining BNT327 with chemo is being investigated in several Phase II and III trials in both 1L and 2L, including a global dose optimization trial. This Phase III trial will further assess the efficacy and safety of BNT327 in combination with chemo for previously untreated pts with ES-SCLC in a global population. **Methods:** Thisglobal, randomized, double-blind, Phase 3 trial (NCT06712355) will enroll ~439 pts with histologically or cytologically confirmed SCLC, who have not received prior systemic therapy for ES-SCLC. Pts will be initially randomized 1:1:1 to receive combination therapy of atezolizumab (1,200 mg IV) plus chemo (etoposide + carboplatin) (Arm 1), BNT327 (2,000 mg IV) plus chemo (Arm 2), or BNT327 (1,400 mg IV) plus chemo (Arm 3) administered Q3W for four cycles, followed by maintenance therapy with atezolizumab (Arm 1) or BNT327 (Arm 2 and Arm 3) Q3W until confirmed disease progression, intolerable toxicity, participant withdrawal, trial termination or up to two years, whichever occurs first. Chemo will be dosed per local treatment guidelines. One of the BNT327 arms (Arm 2 or 3) is expected to be closed upon evolving insights on the optimal dose. Further pts will then be randomized (1:1) into Arm 1 or the remaining BNT327 arm. Stratification includes brain metastasis, liver metastasis, and geography. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), objective response rate, PFS rates and OS rates at defined timepoints, patient-reported outcomes, occurrence of treatment emergent adverse event (TEAEs) and occurrence of dose delay, infusion interruption, and discontinuation due to TEAEs; with efficacy endpoints per RECIST 1.1; safety per CTCAE v5.0. The Phase III trial is currently recruiting pts. Clinical trial information: NCT06712355. Research Sponsor: BioNTech SE.