**BNT113 + pembrolizumab as first-line treatment in patients with unresectable recurrent/metastatic HNSCC: Preliminary safety data from AHEAD-MERIT**


**Background**

HNSCC

- Despite recent advances, such as the use of PD-1 inhibitors, patients with recurrent/metastatic (RM) head and neck squamous cell carcinoma (HNSCC) have poor OS rates.
- HPV is a known cause for HNSCC, with increasing incidence worldwide. Despite a distinct biology compared to HPV- HNSCC, there has been no approved therapy specific for HPV+ HNSCC.

RNA-LPX platform

- RNA Lipoplex (RNA-LPX) is an RNA vaccine administered IV and taken up by dendritic cells (DCs) in lymphoid compartments body-wide.
- The non-nucleoside-modified, uridine-containing mRNA is optimized for translation in immune DCs, and for augmented antigen presentation on human leukocyte antigen (HLA) class I and II receptors.
- RNA-LPX aligns vaccine antigen temporally with co-stimulation through toll-like receptor (TLR) mediated, type-I IFN-driven antiviral immune mechanisms, and results in profound expansion of antigen-specific T cells.

**BNT113 and the AHEAD-MERIT trial**

- BNT113, part of BioNTech’s RNA-LPX platform, encodes the human papillomavirus (HPV) 16 oncoproteins E6 and E7.
- AHEAD-MERIT is an open-label, controlled, multi-site, interventional, 2-arm, Phase II trial of BNT113 in combination with pembrolizumab vs pembrolizumab monotherapy as first line treatment in patients with unresectable recurrent or metastatic HPV+ HNSCC expressing PD-L1 with CPS ≥1.

**A previous exploratory analysis of a trial exploring another RNA-LPX-based vaccine (BNT111) in melanoma (Lipo-MERIT; NCT02410733) showed that BNT111 has a tolerable safety profile**

- Here, we present preliminary safety data in patients from the safety run-in part (Part A) of the trial (data cut-off: 07/2022)

**Trial Objectives**

**Part A**

- **Primary objectives**
  - Safety and tolerability of BNT113 combination in patients with HPV+ HNSCC.
- **Secondary objectives**
  - ODR, DoC, DCR
  - PFS, OS, pharmacodynamic parameters

**Part B**

- **Primary objectives**
  - OS and DCR by BICR

**Methods**

**Trial design**

- **The trial has two parts**
  - **Safety run-in:** A non-randomized part to confirm the safety and tolerability at the selected dose of BNT113 in combination with pembrolizumab
  - **Randomized part:** BNT113 in combination with pembrolizumab versus pembrolizumab monotherapy to generate clinical efficacy and safety data in the first line setting

Dosing:
- BNT113: First 8 vaccinations to be given weekly, then Q3W. Pembrolizumab: Q3W

**Assessments**

- **AEs:** reported by relationship, grade, and seriousness (CTCAE v5.0)
- **Patients undergoing regular CT or MRI imaging assessments of tumors from screening and throughout the trial**
- Blood samples will be taken to characterize pharmacodynamic markers (i.e., cytokine levels, levels of HPV16-specific circulating tumor RNA [cHPV16DNA])

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