TPS6123 Poster Session

RIBBON-UM: Treatment individualisation by EBV stratification in nasopharyngeal carcinoma (NPC): A phase 2, multi-arm umbrella platform trial.

Melvin L.K. Chua, Sze Huey Tan, Enya Ong, Wen Min Chow, Britny H.S. Koh, Jialing Neo, Yoke Lim Soong, Hui Lin Teo, Elise Vong, Mei-Kim Ang, Jens Samol, Darren Wan-Teck Lim; National Cancer Centre Singapore, Duke-NUS Medical School, Singapore, Singapore; Division of Clinical Trials & Epidemiological Sciences, National Cancer Centre Singapore, Singapore, Singapore; National Cancer Centre Singapore, Singapore, Singapore; National Cancer Centre of Singapore, Singapore, Singapore; National Cancer Center of Singapore, Singapore, Singapore; Tan Tock Seng Hospital-National Healthcare Group, Singapore, Singapore; Division of Medical Oncology, National Cancer Centre Singapore, Singapore, Singapore; Department of Medical Oncology, Tan Tock Seng Hospital, Singapore, Singapore; Division of Medical Oncology, National Cancer Centre Singapore, Singapore, Singapore, Singapore

Background: Induction chemotherapy (IC) and chemoradiotherapy (CRT) is the current standard of care (SOC) for locoregionally advanced NPC (LA-NPC). However, CRT alone or CRT and adjuvant chemotherapy (AC) are also first-line SOC options. Plasma Epstein-Barr virus (EBV) DNA is an archetypal biomarker for endemic NPC, and has been assessed for pre-and on-treatment clinical stratification. RIBBON-UM is a phase 2, multi-arm umbrella trial investigating pre- and on-treatment plasma EBV DNA assessment to individualise treatment of patients with LA-NPC. **Methods:** Patients who are newly-diagnosed, biopsy-proven NPC of TNM-stage III-IVA by AJCC/UICC 8th ed and have DETECTABLE EBV DNA pre-treatment are eligible. RIBBON-UM incorporates a 2-tier stratification by TN-status and EBV DNA levels – (1) First, patients will be stratified into low- (LR) and high-risk (HR) based on pre-treatment EBV DNA cut-off 4000 copies/mL AND/OR T4N+ or N2-3 disease; (2) Second, for the HR patients who are assigned to IC (gemcitabine-cisplatin), patients will be further stratified into HR and very-high risk (VHR) depending on their EBV DNA clearance post-3 cycles of IC. RIBBON-UM consists of 3 treatment arms (NCT05517135): Arm I will enroll LR patients (T3N0-1, T4N0 AND EBV DNA $<$4000 copies/mL) to upfront CRT (cisplatin/carboplatin) $\pm$ AC (cisplatin and 5-fluorouracil or capecitabine based on physician's discretion). HR patients (T4N+ OR N2-3 OR EBV DNA $\geq$4,000 copies/mL) will receive upfront IC, and if UNDETECTABLE EBV DNA post-IC, they will be assigned to Arm II – CRT $\pm$ AC. For patients with a DETECTABLE EBV DNA post-IC (VHR), these patients are assigned to Arm III – a single-arm, phase 2 trial investigating experimental AC (NCT06093061), embedded within the RIBBON-UM protocol. Currently, VHR patients enrolled into Arm III will receive CRT + 1-y combined tislelizumab (200 mg IV 3-weekly) and metronomic capecitabine at 650 mg/m^2 bidaily (RIBBON-LA-01, NCT06093061) or 1-y metronomic capecitabine (if they decline). Statistical plan of RIBBON-UM consists of 2 analyses: (1) we will evaluate if our risk-stratification strategy by TN-status and pre- and on-treatment EBV DNA levels improves 2-y disease-free survival (DFS) rate of patients with LA-NPC from 65% (historical) to 75% for the modular platform trial; (2) we hypothesise that AC intensification (Arm III) will improve 2-y DFS of the VHR cohort from 60% (historical) to 75%. 133 and 62 patients are required to test these hypotheses at 5% 1-sided significance level with 80% power, respectively. The risk-stratified treatment individualisation and AC intensification strategies will be deemed successful if 96 of 133 (from Arms I-III) and 44 of 62 patients (Arm III) remain disease-free at 2 y. From Nov 2022 to Jan 2025, we have enrolled 93 and 51 patients into RIBBON-UM and RIBBON-LA-01, respectively. We expect enrolment to RIBBON-UM to complete by Jun 2025. Clinical trial information: NCT05517135, NCT06093061. Research Sponsor: BeiGene; NMRC Singapore Open-Fund Large Collaborative Grant; NMRC Singapore Clinical Trials Grant.