TPS5636 Poster Session

IMMUNORARE[5]: A national platform of 5 academic phase II trials coordinated by Lyon University Hospital to assess the safety and the efficacy of the immunotherapy with domvanalimab + zimberelimab combination in patients with advanced rare cancers—The Gestational Trophoblastic Tumors Cohort.

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Background: For patients with rare cancers, there is an unmet medical need to investigate innovative therapeutics beyond standard first-line treatment. These diseases are rarely evaluated in clinical trials. High-risk gestational trophoblastic tumors (GTT) are treated with polychemotherapy (especially EMA-CO) with high cure rate (~95%). However, patients resistant to polychemotherapy have a poor prognosis, and no validated regimen has been defined. Several case reports suggest that immune checkpoint inhibitors (ICIs) may be active, and a phase II trial with Camrelizumab + Apatinib showed a 50% cure rate. There is a strong rationale for concurrent blockade of the TIGIT and PD1 pathways in this disease. **Methods:** IMMUNORARE[5] (NCT NCT06790706) is a platform of 5 single-arm phase II trials testing the efficacy and tolerability of DOMVANALIMAB (anti-TIGIT) and ZIMBERELIMAB (anti PD-1) in 5 independent cohorts of rare cancers. The trial, sponsored by Lyon University Hospital, will be conducted in 15 French centers, in collaboration with the respective French national reference centers. The gestational trophoblastic tumor cohort, led in collaboration with the French Gestational Trophoblastic Disease Center, will enroll 27 patients with resistance or relapse after at least one line of polychemotherapy (e.g. EP low-dose, BEP, EMA-CO), assessable for biological response with serum hCG (human chorionic gonadotropin). Patients previously treated with immunotherapy are not eligible. Patients will receive intravenous DOMVANALIMAB and ZIMBERELIMAB, every three weeks, until hCG normalization followed by 5 consolidation cycles. The primary objective is the successful hCG normalization rate at 6 months. The secondary objectives are the resistance-free survival, overall survival and tolerance. The trial is designed with a two-stage Simon design, with the possibility of early termination for futility (5% one-sided alpha level, 80% power). The treatment will be considered interesting if the percentage of patients experiencing hCG normalization at 6-months is statistically higher than 35% (H0); 60% is expected (H1). Translational research projects will be developed to unravel the cellular and molecular mechanisms involved in treatment response. Moreover, data from the prospectively implemented database of the French Gestational Trophoblastic Disease Center will be analyzed to create a synthetic historical arm representative of the efficacy of the standard treatments in a similar patient population. Clinical trial information: NCT06790706. Research Sponsor: None.