TPS2693 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 Anaplastic Thyroid Carcinomas Cohort.

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Background: In patients with rare cancers, there is an unmet medical need for investigating innovative therapeutics beyond standard first-line treatment. Indeed, these diseases are rarely assessed in clinical trials. Anaplastic thyroid carcinomas (ATC) represent 2-3 % of thyroid carcinomas, but are responsible for 15-40% of thyroid cancer mortality. Most cases (> 90%) are diagnosed with advanced unresectable disease. In such patients carrying the BRAFV600 mutation (20-30%), the standard 1st-line treatment relies on dabrafenib & trametinib. In patients without BRAF mutation, the 1st line treatment is chemoradiation. There is no validated 2nd line treatment, but immunotherapy combinations seem promising. In DUTHY trial (Durvalumab + tremelimumab), the 6month-OS was 65.6% in ATC. Moreover, TIGIT expression increased during ICI treatment, suggesting potential synergistic effects by simultaneous blockade of TIGIT and PD-1. **Methods:** IMMUNORARE[5] (NCT06790706) is a platform of 5 single arm phase II trials testing the efficacy and safety of DOMVANALIMAB (anti-TIGIT) and ZIMBERELIMAB (anti PD-1) in 5 independent cohorts of rare cancers. The trial, sponsored by Lyon University Hospital, is conducted in 15 French centers, led in partnership with the corresponding French national reference centers. The ATC cohort, led in collaboration with the French network ENDOCAN-TUTHYREF (https://www.tuthyref.com/fr), will enroll 24 patients with either non-mutated BRAF tumours with persistent disease at the first evaluation after chemoradiation or disease progression/relapse after the end of chemoradiation, or with mutated B-RAF tumors in progression after a standard B-RAF inhibitor. Patients will receive intra-venous DOMVANALIMAB and ZIMBERELIMAB, every three weeks, until disease progression. The primary endpoint is the survival rate at 6 months. The secondary objectives are overall response rate and duration of the response, progression-free survival and tolerability. The trial is designed with a two-stage Simon design, with early termination for futility (5% one-sided alpha level, 80% power. The treatment would be considered interesting if the survival rate at 6 months is statistically higher than 25%; 50% is expected. Translational research projects will be developed aiming at deciphering cellular and molecular mechanisms involved in response to treatment. Moreover, data from the prospective database of the ENDOCAN-TUTHYREF network will be investigated to build a synthetic historical arm representative of the efficacy of the standard treatments in a similar population of patients. Clinical trial information: NCT06790706. Research Sponsor: None.