TPS1141 Poster Session

Emiltatug ledadotin (Emi-Le): A B7-H4-directed dolasynthen antibody-drug conjugate (ADC) being investigated in phase 1 dose expansion in patients with triple negative breast cancer who received at least one prior topoisomarase-1 inhibitor ADC.

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Background: Breast cancer is the leading cause of cancer death for women worldwide, with triple-negative breast cancer (TNBC) considered one of the more aggressive breast cancers, accounting for ~15% of all cases. Unfortunately, there remains an unmet medical need for effective and well-tolerated treatments for advanced/metastatic TNBC; in heavily pretreated patients, standard-of-care single-agent chemotherapy has limited efficacy, with response rates of ~5%, PFS ~7 weeks. Emiltatug ledadotin (Emi-Le; XMT-1660) is a B7-H4-directed Dolasynthen ADC designed with a precise, target-optimized drug-to-antibody ratio (DAR 6) and a proprietary auristatin F-HPA microtubule inhibitor payload with controlled bystander effect. The FDA has granted Emi-Le two Fast Track designations for the treatment of adult patients with breast cancer, including patients with TNBC who have previously been treated with topoisomerase-1 inhibitor (topo-1) ADCs. Initial dose escalation clinical data from the ongoing Phase 1 trial at doses ranging from 38.1-67.4 mg/m2 per cycle demonstrated a 23% confirmed response rate in patients with B7-H4 high TNBC who were heavily pretreated all of whom received at least one prior topo-1 ADC. **Methods:** Based on encouraging clinical activity and tolerability data in the initial dose escalation data, the expansion portion (EXP) of the Phase 1 trial has been initiated and is actively enrolling patients. EXP has a Simon 2-stage design and will evaluate two doses in patients with advanced/metastatic TNBC who have received 1-4 prior lines of systemic therapy, including at least one topo-1 ADC. Patients will be evaluated for B7-H4 expression prospectively by IHC and will be stratified into B7-H4 TPS "high" and B7-H4 TPS "low" cohorts. The first EXP dose is 67.4 mg/m2 Q4W. Dose exploration is ongoing to identify a potential second higher EXP dose. The protocol includes the option for multiple additional indications, including HR+/HER2- breast cancer, endometrial cancer, ovarian cancer, and ACC-1. Clinical trial information: NCT05377996. Research Sponsor: Mersana Therapeutics.