TPS2673 Poster Session

SUPRAME: A phase 3 trial comparing IMA203, an engineered T-cell receptor expressing T cell therapy (TCR-T) vs investigator's choice in patients with previously treated advanced cutaneous melanoma.

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Background: Frequent recurrence and limited long-term survival in unresected or metastatic melanoma after relapse from 1L treatment with a checkpoint inhibitor (CPI) highlight the critical need for new therapies that deliver deeper, more durable responses (Knight *Cancers* 2023; Switzer *JCO Oncol Pract* 2022). ACTengine IMA203 is an autologous T cell receptor (TCR)-engineered T cell therapy (TCR-T) targeting PRAME, an intracellular protein displayed as peptide antigen at high density on the surface of multiple solid tumors, including melanoma. IMA203 TCR-T demonstrated a favorable tolerability profile and durable objective responses in heavily-pretreated patients with different tumor types. In melanoma, IMA203 showed 54% confirmed ORR (14/26), 12.1 months mDOR and 6 months mPFS. mOS was not reached at a mFU of 8.6 months (Wermke et al., SMR, Oct 10, 2024). Based on these observations, a registration-enabling randomized phase 3 trial, SUPRAME, was initiated to evaluate IMA203 in 2L patients with advanced cutaneous melanoma after treatment with a CPI. **Methods:** SUPRAME (NCT06743126) is a phase 3, multicenter, open-label, randomized, actively controlled, parallel-group trial that will evaluate the efficacy, safety and tolerability of IMA203 compared to investigator's choice of treatment in patients with previously treated, unresectable or metastatic cutaneous melanoma (incl. acral melanoma). Eligible patients are ≥18yo, HLA-A*02:01-positive, with measurable disease (RECIST v1.1), ECOG PS of 0-1 and disease progression on or after at least one PD-1 inhibitor. Patients with BRAF mutation should have been treated with one prior line of BRAF-directed therapy (± MEK inhibitor) prior to initial eligibility assessment. Patients with asymptomatic stable brain or leptomeningeal metastases will be assessed for eligibility. Patients with active brain metastases or with primary mucosal, uveal melanoma and melanoma of unknown primary are excluded. The study will randomize ~360 patients 1:1. Patients in the experimental arm will undergo leukapheresis to generate the PRAME-specific TCR-T product, IMA203. Following lymphodepletion with cyclophosphamide (500 mg/m^2 x 4 days) and fludarabine (30 mg/m^2 x 4 days), 1-10x10^9 IMA203 TCR-T cells will be administered, followed by low-dose IL-2 (1mio IU daily x5 days, twice daily x5 days). Patients in the control arm will receive approved investigator's choice of standard treatment (nivolumab/relatlimab, nivolumab, ipilimumab, pembrolizumab, lifileucel (US), chemotherapy). The primary efficacy endpoint is BICR-assessed (RECIST v1.1) PFS. Secondary endpoints include OS, ORR, safety and patient-reported outcomes (EORTC QLQ-C30, EQ-5D-5L). The trial will enroll patients in the US and Europe. Clinical trial information: NCT06743126. Research Sponsor: None.