TPS9597 Poster Session

A randomized, phase 2/3 clinical trial investigating RP2 plus nivolumab vs ipilimumab plus nivolumab in immune checkpoint inhibitor-naïve patients with metastatic uveal melanoma.

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Background: Uveal melanoma (UM) is the most common primary intraocular malignancy, accounting for nearly 90% of ocular melanomas and up to 5% of melanomas overall. Approximately 50% of patients (pts) with UM will develop metastatic disease, with the liver being the most common site of metastases (~90%). The prognosis for pts with metastatic UM (mUM) is poor, with a median overall survival (OS) of approximately 1 year. Effective treatment options for mUM are limited as it responds poorly to single-agent immune checkpoint inhibitors (ICIs; <10% response rate). Response rates are slightly higher with combination therapies (12%–18%), but often at the expense of increased toxicity. Tebentafusp is FDA approved for mUM based on survival benefit; however, its use is restricted to pts who are HLA-A*02:01 positive, and only ~10% of pts achieve an objective response. RP2 is a selectively replication-competent herpes simplex virus type 1–based oncolytic immunotherapy expressing GM-CSF, a fusogenic glycoprotein (GALV-GP-R–), and an anti–CTLA-4 antibody-like molecule. Prior phase 1 preliminary clinical data of RP2 as monotherapy or in combination with nivolumab (nivo) demonstrated a promising safety profile and anti-tumor activity with an ORR of 29.4% in 17 patients with mUM, most of whom had received prior ICIs. This study will assess the efficacy and safety of RP2 + nivo vs ipilimumab (ipi) + nivo in pts with ICI-naïve mUM (NCT06581406; RP2-202). **Methods:** This is a randomized, controlled, phase 2/3 study. Key eligibility criteria include age ≥18 years and confirmed unresectable mUM with lesions amenable to injection. Pts with metastatic disease who have had prior exposure to ICIs since the time of UM diagnosis, involvement of >33.3% of the liver, or a history of prior liver- or lesion-directed therapy are not eligible for enrollment. Enrolled pts (N = ~280) will be randomized 1:1 to receive either RP2 + nivo or ipi + nivo. In the RP2 + nivo arm, RP2 will be given intratumorally initially at 1×10^6 PFU/mL, then every 2 weeks (Q2W) at 1×10^7 PFU/mL for 7 doses in combination with intravenous (IV) nivo (240 mg). In the ipi + nivo arm, pts will receive IV ipi (3 mg/kg) and IV nivo (1 mg/kg) Q3W for 4 doses. Pts in both arms may then receive IV nivo at 240 mg Q2W or 480 mg Q4W for up to 2 years from the first dose. The co-primary endpoints are OS and progression-free survival by independent central review using RECIST 1.1. Secondary endpoints are overall response rate, duration of response, disease control rate, clinical benefit rate, duration of clinical benefit, and safety, including incidence of treatment-emergent adverse events (AEs), serious AEs, and immune-mediated AEs. Clinical trial information: NCT06581406. Research Sponsor: Replimune, Inc.