TPS9599 Poster Session

A randomized, controlled, multicenter, phase 3 study of vusolimogene oderparepvec combined with nivolumab vs treatment of physician's choice in patients with advanced melanoma that has progressed on anti–PD-1 and anti–CTLA-4 therapy (IGNYTE-3).

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Background: Melanoma is the fifth most common cancer, with ~100,000 new cases and ~8000 related deaths estimated in the US for 2024. First-line systemic treatment with immune checkpoint inhibitors improves the objective response rate (ORR) and extends progression-free survival (PFS) and overall survival (OS) for patients with advanced disease. Among available treatments, combination anti–PD-1 (nivolumab) + anti–CTLA-4 (ipilimumab) therapy is associated with the highest ORR and best PFS and OS. However, only ~50% of patients respond to treatment, and limited options exist for patients whose melanoma progresses following anti–PD-1–based therapy. Vusolimogene oderparepvec (VO; also known as RP1) is a selectively replication-competent herpes simplex virus type 1–based oncolytic immunotherapy that expresses human granulocyte-macrophage colony-stimulating factor and a fusogenic glycoprotein (GALV-GP-R–). Data from a registration-intended cohort of the IGNYTE study (NCT03767348) showed that intratumoral VO + intravenous nivolumab was well tolerated and demonstrated durable, clinically meaningful antitumor activity (ORR, 32.9% per independent central review using Response Evaluation Criteria in Solid Tumors 1.1) in patients with advanced melanoma and confirmed progression on prior anti–PD-1 therapy. IGNYTE-3 will evaluate the OS and clinical benefit of VO + nivolumab for patients with advanced cutaneous melanoma whose disease has progressed after anti–PD-1 and anti–CTLA-4 therapy (or who are ineligible for anti–CTLA-4 therapy) vs physician's choice. **Methods:** IGNYTE-3 (NCT06264180) is a global, randomized, controlled, multicenter, phase 3 trial (currently recruiting). Key eligibility criteria include age ≥12 years; stage IIIb–IV/M1a–M1d cutaneous melanoma; disease progression on ≥8 weeks of an anti–PD-1 and anti–CTLA-4 treatment (administered in combination or in sequence, with anti–PD-1 last); ≥1 measurable and injectable tumor (≥1 cm); and adequate hematologic, hepatic, and renal function. Patients who are not candidates for anti–CTLA-4 therapy may enroll following progression on anti–PD-1 therapy alone. Patients with BRAF V600-mutant melanoma must have received anti-BRAF ± anti-MEK targeted therapy prior to enrollment. Patients (N = ~400) will receive VO + nivolumab or physician's choice (nivolumab + relatlimab, anti–PD-1 monotherapy rechallenge [nivolumab or pembrolizumab], or single-agent chemotherapy [dacarbazine, temozolomide, or paclitaxel/albumin-bound paclitaxel]). The primary endpoint of the study is OS; the key secondary endpoints are PFS and ORR per RECIST 1.1. Clinical trial information: NCT06264180. Research Sponsor: Replimune, Inc.