T-4

Trial-in-Progress: A Phase 2 Study of ONC206 (JZP3507) in Patients With Advanced Pheochromocytoma and Paraganglioma

Vivek K. Narayan[1], Justin P. Annes[2], Wanxing Chai-Ho[3], Mabel Ryder[4], Nikolaos A. Trikalinos[5], Francis P. Worden[6], Samuel C. Ramage[7], Carlos Mayo[7], Heloisa P. Soares[8]

[1]Division of Hematology Oncology, Perelman Center for Advanced Medicine, University of Pennsylvania, Philadelphia, PA, USA; [2]Department of Medicine, Division of Endocrinology and Endocrine Oncology, Stanford School of Medicine, Stanford, CA, USA; [3]Department of Medicine, Division of Hematology/Oncology, David Geffen School of Medicine, and Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [4]Department of Endocrinology and Medical Oncology, Mayo Clinic Comprehensive Cancer Center, Rochester, MN, USA; [5]Department of Internal Medicine, Division of Oncology, Washington University School of Medicine and Siteman Cancer Center, St. Louis, MO, USA; [6]Department of Internal Medicine, Division of Hematology/Oncology, University of Michigan Cancer Center, Ann Arbor, MI, USA; [7]Jazz Pharmaceuticals, Philadelphia, PA, USA; [8]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA

BACKGROUND

Effective treatment options for patients with metastatic pheochromocytoma and paraganglioma (PCPG) remain limited, highlighting a significant unmet therapeutic need. JZP3507 (formerly ONC206), an oral, brain-penetrant second generation imipridone with nanomolar potency, acts as a selective ClpP agonist and DRD2/3 antagonist. Encouraging clinical responses have been demonstrated with dordaviprone in patients with advanced paraganglioma. Similarly, in vitro models have shown efficacy with JZP3507 across multiple tumor types, including PCPG. JZP3507 has been shown to disrupt mitochondrial function and induce apoptosis of tumor cells. Phase 1 clinical trials demonstrated the safety and tolerability of multiple doses and schedules of JZP3507 in patients with advanced CNS tumors, with most treatment-related adverse events being mild to moderate, including fatigue, lymphocyte count decrease, and vomiting. This study will assess the safety and efficacy of JZP3507 in patients with locally advanced or metastatic PCPG.

METHODS

This is an open-label, dose-optimization, multicenter, two-stage phase 2 clinical study (NCT07282587). Eligible patients include those aged ≥18 years with histologically confirmed unresectable PCPG, measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, an Eastern Cooperative Oncology Group (ECOG) Performance

Status of 0 to 2, and adequately controlled blood pressure (≤150/90 mm Hg) and who have exhausted or declined further standard systemic treatments. Patients with active cardiac disease, active infection requiring treatment, or previous exposure to JZP3507 or dordaviprone are not eligible. In stage 1, 150 mg JZP3507 will be administered twice daily on 3 consecutive days per week in 28-day cycles. If stage 1 meets the pre-specified response threshold (confirmed response in >6 patients), the study will proceed to stage 2, and participants will be randomized 1:1 to one of two JZP3507 dose levels (to be determined post stage 1). Treatment will continue until disease progression, unacceptable toxicity, or patient/physician request to discontinue treatment. The primary endpoint is overall response rate (patients with confirmed complete or partial response) by RECIST v1.1. Imaging will be collected pre-baseline, at baseline, and every 12 weeks (±7 days) thereafter until disease progression per RECIST v1.1. Key secondary endpoints include evaluation of PCPG growth and symptoms (including progression-free survival, overall survival, antihypertensive medication dosing, and biochemical disease markers [plasma metanephrines]) and safety, pharmacokinetics, and quality of life. Exploratory endpoints include incidence and time to new metastases by location and subsequent anticancer therapy. Total anticipated enrollment is 90 patients (as of June 1, 2026, 8 patients have been enrolled).

RESULTS

Non-applicable

CONCLUSIONS

Non-applicable

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