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Trial-in-Progress: A Phase 2 Study of ONC206 in Patients with Advanced Pheochromocytoma and Paraganglioma

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BACKGROUND

Treatment options for patients with metastatic pheochromocytoma and paraganglioma (PCPG) are limited following surgical resection and radiotherapy. ONC206 is an inhibitor of dopamine receptor D2 (DRD2) and an agonist of caseinolytic protease proteolytic subunit (ClpP). This small molecule is a potent derivative of dordaviprone that was previously reported to induce responses in patients with PCPG. In vitro models have demonstrated ONC206 efficacy across multiple tumor types, including PCPG. Downstream effects of ONC206 in tumors cells induce disruption of mitochondrial function, degradation of mitochondrial enzymes commonly altered in PCPG such as succinate dehydrogenase, and induction of apoptosis. Phase 1 clinical trials have evaluated the safety and tolerability of multiple doses and schedules of ONC206 in patients with advanced CNS tumors.

METHODS

This open-label, multicenter, two-stage Phase 2 clinical study will evaluate efficacy and safety of ONC206 in adult patients with advanced PCPG who have locally advanced or metastatic disease and have exhausted or declined available therapy. Eligible patients have histologically confirmed PCPG, are ineligible for curative surgery, and have failed prior PCPG therapy or declined further standard systemic therapies. The primary objective is to determine the antitumor activity of ONC206 as assessed by overall response rate by RECIST v1.1 criteria. Imaging will be collected pre-baseline, baseline, and every 12 weeks (±7 days) thereafter until disease progression. Key secondary objectives include evaluating the effect of ONC206 on PCPG growth trajectory, antihypertensive medication use and dosing, biochemical disease markers (plasma metanephrines), safety, pharmacokinetic parameters, and quality of life assessments. Total anticipated enrollment is 90 patients.

RESULTS

N/A

CONCLUSIONS

N/A

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