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An Open-Label, Phase 1b/2 study of Surufatinib in Combination with Tislelizumab in Patients with Advanced Neuroendocrine Tumors

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BACKGROUND

Surufatinib, an oral small molecule tyrosine kinase inhibitor, selectively inhibits vascular endothelial growth factor receptor 1, 2, and 3; fibroblast growth factor receptor 1; and colony-stimulating factor 1 receptor. Tislelizumab is a humanized immunoglobulin G4-variant anti-programmed cell death protein-1 monoclonal antibody. Combining surufatinib and tislelizumab may have synergistic effects, where inhibition of angiogenesis and stimulation of an immune response may enhance overall antitumor activity compared to each agent alone.

METHODS

This is an open-label, Phase 1b/2 dose escalation (ESC)/expansion (EXP) study (NCT04579757) to determine the recommended Phase 2 dose (RP2D) and/or the maximum tolerated dose for the combination of surufatinib and tislelizumab in patients with advanced solid tumors and to explore the preliminary antitumor activity of the combination. ESC used a 3+3 design at 2 surufatinib dose levels 250 mg and 300 mg once daily. In EXP, patients received surufatinib orally once daily at the RP2D and tislelizumab 200 mg intravenously every 3 weeks. Findings from 2 EXP cohorts of thoracic and gastroenteropancreatic (GEP) neuroendocrine tumors (NETs) are reported here.

RESULTS

The surufatinib RP2D established in ESC was 300 mg once daily. Twenty-nine patients with NETs were enrolled in EXP (9 thoracic NET, 20 GEP NET). All patients had received prior anticancer treatment: 25 (86.2%) somatostatin analogs, 14 (48.3%) radionuclide therapy, 10 (34.5%) everolimus, and 2 (6.9%) sunitinib. No patient demonstrated a complete response. Partial responses were seen in 5 (17.2%) patients (2 small bowel and 1 each pancreas, lung, and unknown); and stable disease was seen in 10 (34.5%) patients. The objective response rate was 11.1% (95% confidence interval [CI]: 0.3, 48.2) for the thoracic NET cohort and 20.0% (95% CI: 5.7, 43.70) for the GEP NET cohort (including 1 unconfirmed partial response). All 29 (100.0%) patients reported at least 1 treatment emergent adverse event (TEAE); 20 (69.0%) patients reported TEAEs \geq grade 3.

The most common TEAEs of any grade were increased aspartate aminotransferase (AST) (51.7%), nausea and hypertension (44.8% each), decreased appetite and fatigue (41.4% each), and increased alanine aminotransferase (ALT) (34.5%). The most common \geq grade 3 TEAEs were increased AST in 6 (20.7%) patients and increased ALT in 5 (17.2%) patients. The most common TEAEs leading to surufatinib dose reduction were increased AST and ALT in 2 (10%) patients each in the GEP NET cohort.

CONCLUSIONS

The combination of surufatinib and tislelizumab demonstrated antitumor activity in pretreated US patients with thoracic and GEP NETs with a manageable safety profile.

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