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A Phase 2 Study of Surufatinib in Combination with Toripalimab in Patients with Advanced Neuroendocrine Carcinoma

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BACKGROUND: Surufatinib is a multi-kinase inhibitor of VEGFR1-3, FGFR1 and CSF-1R. Toripalimab is a PD-1 inhibitor. Combination therapy of the agents has showed promising antitumor activity for the 2L treatment of advanced neuroendocrine carcinoma (NEC). This study reports an updated analysis to further investigate the efficacy of the combination.

METHODS: In this multicenter, open-label, single-arm phase 2 study (NCT04169672), eligible patients with advanced NEC who failed 1L chemotherapy received 3-week cycles of 250mg surufatinib (orally, QD) plus 240mg toripalimab (IV, Q3W), until disease progression, death, or unacceptable toxicity, but for up to 24 months with toripalimab. The primary endpoint was objective response rate (ORR) per RECIST 1.1.

RESULTS: Twenty-one eligible patients (81.0% primary lesion in extra-pulmonary NECs, 76.2% PD-L1 CPS<10, 85.7% Ki-67 >55%) were enrolled. Median treatment

duration of both surufatinib and toripalimab was 4 months. At this updated data cutoff (June 15, 2021), 5 patients had confirmed partial response and 10 patients had stable disease among evaluable patients (n=21). The confirmed ORR was 23.8% (95%CI: 8.22%-47.17%) and the DCR was 71.4% (95%CI: 47.82%-88.72%). The median DoR of the responders was 4.11 months (95%CI: 2.99-NR). Median PFS was 4.14 months (95%CI: 1.45-5.45), and median OS was 10.18 months (95%CI: 9.03-NR). Nine (42.9%) patients had grade ≥ 3 treatment-related adverse events (TRAEs), with hyperglycemia (3 [14.3%]), hypertension (2 [9.5%]) and hypertriglyceridemia (2 [9.5%]) the most common (>2 patients). Nine (42.9%) or 3 (14.3%) patients had surufatinib or toripalimab interruption, due to TRAEs, respectively, however no TRAEs leading to treatment discontinuation or treatment-related deaths were reported.

CONCLUSION: Surufatinib plus toripalimab demonstrated clinically meaningful anti-tumor activity, and is a potential treatment option for 2L treatment of NEC that should be further investigated. A randomized phase 3 study is initiated to further confirm the efficacy of this combination therapy in 2L NEC.

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