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NEUROENDOCRINE TUMOURS

1307O Efficacy of lenvatinib in patients with advanced pancreatic (panNETs) and gastrointestinal (giNETs) grade 1/2 (G1/G2) neuroendocrine tumors: Results of the international phase II TALENT trial (GETNE 1509)

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Background: Patients (pts) with advanced well-differentiated (G1/G2) NETs have limited treatment options. Everolimus (E) and sunitinib (S) are approved with overall response rates (ORR) <10% with no demonstrated activity after progression (PD) to prior targeted agents (TA). Lenvatinib is a multikinase inhibitor with potent affinity against VEGFR1-3 and FGFR1-4 that may increase efficacy and revert primary and acquired resistance to TA. We conducted a phase II study to evaluate the efficacy of lenvatinib in panNETS and giNETs.

Methods: This is a prospective phase II study with two cohorts of pts with advanced G1/G2 panNETs (cohort A) and giNETs (cohort B). All pts had documented PD by RECIST prior inclusion. In cohort A, pts should have PD to E or S, regardless prior therapy with somatostatin analogs (SSAs) or chemotherapy (CHT), and in cohort B after PD on SSAs. Pts were treated with lenvatinib at 24 mg qd until PD or intolerable toxicity. The primary endpoint was ORR by RECIST 1.1 upon central radiology review. With 55 pts in each arm, our study was powered to identify an ORR with lenvatinib of $\geq$ 25% with 90% power and 5% α-error.

Results: We included 111 pts (55 panNETs and 56 giNETs). Median age was 59-y, 51% were male and 70% were G2. For panNETs, 32% of pts were previously treated with CHT, 87% with SSAs, 70% with E and 30% with S. ORR by central radiology assessment was 29%, 40% for panNETs and 18.5% for giNETs. Stable disease was observed as best response in 55.7% of panNETs and 76% of giNETs. With a median follow-up of 11 months, estimated median progression-free survival (PFS) for panNETs was 14.2 months (95% CI 11.4-NR) and 17.6 months (95% CI 11.5-NR) for giNETs. Adverse events (AEs) were mild to moderate in 90% of pts, being fatigue, diarrhea and hypertension the most frequent. Grade 3/4 AEs were reported in 10% of pts.

Conclusions: Lenvatinib showed significant antitumor activity and a favorable toxicity profile in progressive advanced NETs. This is the highest reported ORR with a TA confirmed by central radiology assessment in panNETs and giNETs with promising PFS in a pretreated population; further evaluation is warranted.

Clinical trial identification: NCT02678780.

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