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Subgroup Analysis by Ki-67 and Baseline CgA of the Randomized, Placebo-controlled Phase 3 Study of Surufatinib in Advanced Well-differentiated Pancreatic Neuroendocrine Tumors (SANET-p)

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BACKGROUND: In the phase 3 SANET-p trial (NCT02589821), surufatinib significantly increased progression-free survival (PFS) versus placebo in patients with progressive, well-differentiated, advanced pancreatic neuroendocrine tumors (NETs). Here we report the relationship of Ki-67 and baseline Chromogranin A (CgA) on efficacy outcomes.

METHODS: Overall, 172 eligible patients were randomized (2:1) to surufatinib or placebo. Investigator-assessed PFS and objective response rate (ORR) per RECIST 1.1 were used for the analysis. The post-hoc subgroup analyses were performed on Ki-67 subcategory: <5% (n = 40 vs 21), 5-10% (n = 57 vs 31), >10% (n = 16 vs 7), and baseline CgA subcategory: ≤2 times of upper limit of normal (ULN) (n = 59 vs 31), >2 _ ULN (n = 44 vs 24).

RESULTS: In the intent-to-treat population, surufatinib was superior to placebo, median PFS (mPFS) of 10.9 vs 3.7 months (mo) (p = 0.0011), with a stratified HR of 0.491 (95% CI: 0.319, 0.755). mPFS was significantly longer with surufatinib than that with placebo in subgroups of Ki-67 5-10% (11.0 vs 3.7 mo, HR = 0.33, p= 0.0002), Ki-67 >10% (11.1 vs 2.8 mo, HR = 0.04, p = 0.0003) and CgA >2 _ ULN (11.0 vs 3.7 mo, HR = 0.36, p = 0.0036). ORRs in the subgroups of Ki-67 <5%, 5-10%, and >10% with surufatinib were 15.8%, 24.0% and 12.5% respectively. There was only one partial response in the placebo arm (with Ki-67 <5%). ORRs in the subgroups of CgA ≤2 _ ULN and >2 _ ULN with surufatinib were 18.9% and 21.4% (with only one partial response in the CgA ≤2 _ ULN subgroup).

CONCLUSION: Surufatinib showed substantial improvement in PFS compared to placebo in patients with advanced, progressive, well-differentiated pancreatic NETs, irrespective of Ki-67 expression levels or baseline CgA.

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