Updated safety, efficacy and PK results from an open-label, multicenter, Phase I/II study of avapritinib in Chinese patients with unresectable or metastatic gastrointestinal stromal tumors (GIST)

Background: More than 85% of GIST patients (pts) have tumors associated with KIT/PDGFRA mutations. Avapritinib is a potent, selective, small molecule KIT/PDGFRA inhibitor and has been approved in US for pts with GIST harboring PDGFRA exon 18 mutation. However, these pts have no standard of care in China. This abstract reports safety, efficacy and PK results of avapritinib in Chinese pts.

Methods: Adult pts with unresectable or metastatic GIST were enrolled into the 2-part, open-label, phase I/II bridging study. The study had 2 parts: dose escalation (phase I, 200 mg and 300 mg once daily [QD]) and dose expansion (phase II, pts with PDGFRA D842V-mutant and 3L/4L+ GIST). Primary endpoints were recommended phase 2 dose (RP2D) and safety in the dose-escalation part; overall response and safety in the dose-expansion part.

Results: As of 31 Jul 2020, 60 pts were treated with avapritinib QD with 12 pts treated at a starting dose of 200 mg or 300 mg (6 per group) in phase I, 48 pts with D842V (20) and 3L+ (28) were treated at 300 mg QD (RP2D) in phase II. Forty pts remained on treatment; median treatment duration was 25.4 weeks. Treatment-related G3-4 AEs occurred in 41 of 60 pts, the most common being anemia (32%). There were no treatment-related deaths. As assessed by investigators, of the 20 pts with D842V-mutant, 15 pts had PR leading to a 75% ORR; of the 23 pts with 4L+ GIST, 9 (39%) pts had an objective response, with 1 (4%) CR and 8 (35%) PRs. Most responders (D842V-mutant [13] and 4L+ GIST [7]) remain in remission. The mPFS for D842V-mutant was not reached, mPFS for 4L+ GIST was 5.5 months. Avapritinib was rapidly absorbed (mT_{max}: 2.0 h) and drug exposure increased proportionally with dose at the steady-state. The mean $t_{1/2}$ ranged 30.9-42.2 h, supporting QD dosing.

Conclusion(s): Avapritinib appears generally well-tolerated at 200 mg and 300 mg QD in Chinese pts. 300 mg QD was determined as RP2D for Chinese pts. Our data show that avapritinib demonstrated strong antitumor activity in pts with PDGFRA D842V-mutant and 4L+ GIST, making it an important potential new treatment option for the population.

Clinical Trial identification:NCT04254939