预览

主题分类:E-胃肠肿瘤>E3-其他>

Safety, pharmacokinetics (PK) and efficacy results from an open-label, multicenter, Phase 1/2 study of avapritinib in Chinese patients (pts) with unresectable or metastatic gastrointestinal stromal tumors (GIST)

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目的: Avapritinib is a potent, selective, small-molecule inhibitor that targets KIT/PDGFRA mutants. On 9Jan2020, U.S. FDA approved avapritinib for adults with unresectable or metastatic GIST harboring PDGFRA exon 18 mutation, including D842V mutations. This study evaluates the safety, PK and anti-tumor activity of avapritinib from the dose escalation (phase 1) and expansion (phase 2) phases of the bridging study in Chinese pts with GIST.

方法: The dose escalation phase determined DLT and recommended phase 2 dose (RP2D). The safety, PK and anti-tumor activity of avapritinib was assessed from both phases (50 pts for safety, 8 pts with D842V mutation and 23 4L+ pts for efficacy).

结果: As of 31Mar2020, a total of 50 pts were enrolled and received at least 1 dose of avapritinib. Phase 1 included 6 pts at 200 mg and 6 pts at 300 mg once daily (QD). DLT were not observed and the RP2D was determined to be 300 mg QD. Phase 2 enrolled 38

pts including 10 with D842V mutation and 28 3L+ pts (including 20 4L+ pts). For all 50 pts, the median treatment duration was 13.9 weeks. Treatment-related adverse events (TRAEs) were reported in 48 pts (96%) and 23 pts (46%) reported ≥Grade3 TRAEs. The most common TRAEs were anemia (n=32, 64%) and blood bilirubin increased (n=32, 64%). 14 pts (28%) reported Serious AEs (SAEs) during the study, 4 pts (8%) reported treatment-related SAEs including anemia (n=2), face edema, pleural effusion and pneumonia (n=1 for each). No TRAE leading to study drug discontinuation or death was reported.
Avapritinib was rapidly absorbed (T_{max}: ~2 h), exposure increased with dose and half life ($t_{1/2}$) was ~40 h, thereby supporting QD dosing. The investigator-assessed objective response rate (ORR, unconfirmed) per mRECIST v1.1 at 300 mg QD (Phase 1/2 pts) was 62.5% (5 partial response [PR] and 3 stable disease [SD]) in 8 response-evaluable pts harboring PDGFRA D842V mutation and 26.1% (6 PR and 13 SD) for the 23 4L+ response-evaluable pts, respectively.

结论: Avapritinib was well tolerated and the RP2D was determined as 300 mg QD. Avapritinib demonstrated strong anti-tumor activity in Chinese GIST pts, especially those with PDGFR D842V mutation.

关键字: Platelet-Derived Growth Factor,Gastrointestinal Stromal Tumor,Bridging study
附件: 无

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