SARCOMA

1603O Initial results of phase I study of DCC-2618, a broad-spectrum KIT and PDGFRα inhibitor, in patients (pts) with gastrointestinal stromal tumor (GIST) by number of prior regimens


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Background: DCC-2618, a kinase switch control inhibitor, broadly inhibits mutations in KIT exons 9, 11, 13, 14, 17 and 18. Based on clinical activity observed in heavily pretreated GIST pts in a Phase 1 study, DCC-2618 is being evaluated in a Phase 3 study, INVICTUS (NCT03353753), in ≥ 4th line pts. Given the breadth of inhibition of KIT mutations and favorable tolerability profile, the Phase 1 study included expansion cohorts to assess clinical benefit in ≥ 1st and 3rd line GIST pts in advance of the expected initiation of a second Phase 3 study in ≥ 2nd line GIST pts by the end of 2018.

Methods: The Phase 1 study includes a dose-escalation component testing oral DCC-2618 dosed QD or BID in 28 day cycles and an expansion phase using the RP2D of 150 mg QD in 6 cohorts, including cohorts for GIST pts based on prior regimens (≥ 1st/3rd, 4th/4-th). RECIST response assessments based on local assessment of CT scans were performed every 2 cycles.

Results: At the cut off of April 18, 150 GIST pts were enrolled at dose levels of ≥ 100 mg/d with KIT (141 pts) or PDGFRα- (8 pts) -driven GIST. One pt had SDH-deficient GIST. 114 GIST pts were treated at the 150 mg QD dose, including 19, 27, and 68 pts who previously received 1, 2 or ≥ 3 prior lines of therapy, respectively. For the 114 GIST pts, ORR was 14%, 3-month DCR was 70%, mPFS was 24 weeks with 56% of...
the pts censored. For the 46 evaluable pts in 2nd/3rd line, ORR was 22%, 3-month DCR was 81% and mPFS was 36 weeks with 61% of the pts censored. Updated ORR, DCR and mPFS will be presented. Grade 3/4 adverse effects (regardless of attribution, in >1 pt) for all 114 pts treated at 150 mg QD included asymptomatic lipase increase 11, anemia 4, hypertension 3, blood bilirubin increased 3, diarrhea 2, abdominal pain 2, back pain 2, hypophosphatemia 2, hyponatremia 2, hyperkalemia 2.

Conclusions: DCC-2618 demonstrated encouraging clinical benefit and a favorable tolerability profile in GIST pts treated in the 2nd line or later. Clinical benefit as measured by ORR, DCR and mPFS was greater in 2nd/3rd line pts compared to more heavily pretreated pts. Preliminary data from the Phase 1 expansion supports further testing in the planned Phase 3 study in 2nd line GIST.

Clinical trial identification: NCT02571036.

Legal entity responsible for the study: Deciphera Pharmaceuticals, Inc.