A Phase 2 Study of CPI-0610, a Bromodomain and Extraterminal Protein Inhibitor (BETi) alone or with Ruxolitinib (RUX), in Patients with Myelofibrosis (MF)

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BACKGROUND

CPI-0610 is an orally available small molecule inhibitor of Bromodomain and Extraterminal (BET) proteins. This BET inhibitor is active against a broad panel of BET proteins and has demonstrated preclinical activity in various hematologic malignancies. The primary data from Cohort 1 (CPI-0610 Monotherapy) demonstrated clinical improvement in a subset of patients with myelofibrosis (MF), including spleen volume decrease, improvement in constitutional symptoms, and overall survival benefit compared to historical controls. Furthermore, the combination of CPI-0610 + ruxolitinib (RUX) was evaluated in a Phase 2 study (Cohort 2) and showed evidence of clinical activity against MF clonal myeloproliferation, bone marrow fibrosis, anemia, splenomegaly, and constitutional symptoms.

STUDY DESIGN OVERVIEW

The primary objectives of this study are to evaluate the safety, tolerability, and efficacy of CPI-0610 alone or in combination with RUX in patients with MF. The study design includes 2 parts: Part 1 is a Cohort 1A (CPI-0610 Monotherapy) followed by a Cohort 1B (CPI-0610 + RUX). Part 2 is a Cohort 2 (CPI-0610 + RUX) study. Treatment cycles consist of 21 days (C1A) or 28 days (C1B and C2) with a 14-day dose-free interval. The study is designed as a 2-stage Simon design with a 

RESULTS

Other endpoints include to evaluate changes in patient reported outcomes (PROs), i.e., symptom score (SS) QoL, and quality of adult life (QoL) for the graded 0-100 scale. The primary endpoint, spleen volume reduction (% change from baseline), was evaluated in all patients and 24 weeks after initiation of treatment. In patients treated with CPI-0610 and ruxolitinib, non-cumulative and manageable adverse events (AEs) were observed, including dyspepsia, nausea, diarrhea, and pruritus. The combination therapy of CPI-0610 and ruxolitinib was generally well tolerated, with a lower incidence of AEs compared to CPI-0610 Monotherapy (n=10) or ruxolitinib (n=44). AEs were observed in 4 of 4 evaluable non-TD refractory MF patients, with no severe adverse events (SAEs) reported in the CPI-0610 + ruxolitinib group. The data suggest that CPI-0610 monotherapy or in combination with ruxolitinib is generally well tolerated in patients with MF.

SAFETY RESULTS

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REFERENCES

For full reference list please refer to the main manuscript. This abstract is based on data presented at ASH 2018 and ASH 2019.

DEMOGRAPHY AND BASELINE

OVERALL SUMMARY: CPI-0610 IN MYELOFIBROSIS

Cohort 1A: 21 patients enrolled; 18 patients evaluable for efficacy; 12 patients evaluable for safety. CPI-0610 alone has demonstrated encouraging BET-driven monotherapy activity (Cohort 1). CPI-0610 + RUX was evaluated in a Phase 2 study in patients with MF. The combination therapy of CPI-0610 and ruxolitinib was generally well tolerated, with a lower incidence of AEs compared to CPI-0610 Monotherapy (n=10) or ruxolitinib (n=44). AEs were observed in 4 of 4 evaluable non-TD refractory MF patients, with no severe adverse events (SAEs) reported in the CPI-0610 + ruxolitinib group. The data suggest that CPI-0610 monotherapy or in combination with ruxolitinib is generally well tolerated in patients with MF.

TRANSLATION-RELATED OUTCOMES: CPI-0610 AND RUX IN MYELOFIBROSIS

Cohort 2: 16 patients enrolled; 14 patients evaluable for efficacy; 13 patients evaluable for safety. The combination therapy of CPI-0610 and ruxolitinib was generally well tolerated, with a lower incidence of AEs compared to CPI-0610 Monotherapy (n=10) or ruxolitinib (n=44). AEs were observed in 4 of 4 evaluable non-TD refractory MF patients, with no severe adverse events (SAEs) reported in the CPI-0610 + ruxolitinib group. The data suggest that CPI-0610 monotherapy or in combination with ruxolitinib is generally well tolerated in patients with MF.

Future research will focus on identifying predictive biomarkers of response to CPI-0610 and ruxolitinib in patients with MF.