Abstract: PB2845

Title: JAB-8263, A POTENT BET INHIBITOR, IN MYELOFIBROSIS AND OTHER ADVANCED MYELOID NEOPLASMS: RESULTS FROM A PHASE 1/2A STUDY

Abstract Type: Publication Only

Topic: Myeloproliferative neoplasms - Clinical

Background:

Bromodomain and extra-terminal (BET) proteins play roles in epigenetic regulation in critical genes involved in inflammation, and various oncogenic processes. JAB-8263 is a high potent, orally available BET inhibitor that is being evaluated as monotherapy in patients with solid tumors and hematological malignancies in a phase 1/2a study (NCT04686682).

Aims:

To evaluate the safety and efficacy of JAB-8283 in patients with recurrent/refractory acute myeloid leukemia (R/R AML) and myelofibrosis (MF).

Methods:

In this ongoing phase 1/2a, dose-escalation/expansion study, patients received JAB-8263 from 0.025 mg once every 2 days (Q2D) to 0.4 mg once daily (QD). The key criteria included: the patients with R/R AML or MF (spleen volume ≥450 cm3), ECOG PS ≤2; and Dynamic International Prognostic score ≥ intermediate-1. Primary objectives of phase I part are safety, tolerability, and determination of the maximum tolerated dose (MTD) and/or recommended Phase 2 dose (RP2D) of JAB-8263.

Results:

As of Feb 2, 2024, 28 patients (19 patients with AML, 9 patients with MF) were enrolled in 8 dose levels. One MF patient in 0.4mg QD experienced a DLT with Grade 3 ALT/AST increase. The most common (>10%) treatment-related adverse events (TRAE) were nausea, blood bilirubin increased, platelet count decreased, alanine aminotransferase increased, aspartate aminotransferase increased, diarrhea, vomiting, and anemia. Mild GI toxicities were observed.

In MF, six patients had at least one post treatment assessment for spleen volume reduction (SVR) and total symptom score (TSS) at week 12. All six patients had improvement in SVR (mean reduction of 18.2%, range: 9.45%-34.88%). One patient achieved SVR 34.88% at 12 weeks. The mean TSS reduction percentage at week 12 was 41% (range: 0-79.4%). Two patients (33.3%) achieved greater than 50% reduction in TSS. Three patients have yet to reach the first imaging evaluation. All nine MF patients are ongoing in the study.

Summary/Conclusion:

The preliminary results indicate that JAB-8263 is well tolerated in patients and has clinical activity in MF patients. The spleen size reduction and symptomatic improvement were observed. JAB-8263 will be further explored in MF.

Keywords: Epigenetic, Myeloproliferative disorder, Myelofibrosis