LONG TERM SAFETY OF MOMELOTINIB IN JAKI naive AND PREVIOUSLY JAKI TREATED INTERMEDIATE/HIGH RISK MYELOFIBROSIS PATIENTS

METHODS

Data were analyzed from two Phase 3 trials of patients with MF [9] (refer to poster #EP1103 for schematics):
- SIMPLIFY-1 (S1): 1:1 Randomized Treatment (RT, double-blind) of MMB vs ruxolitinib (RUX) for 24 weeks in 423 JAKI-naive patients, followed by open-label RT (EMM). Trial duration = 4.6 years.
- SIMPLIFY-2 (S2), 2:1 RT of MMB vs best available therapy (BAT [88% RUX]) for 24 weeks in 156 anemic or thrombocytopenic-poor RUX-treated patients, followed by BAT duration + 4.8 years.

An extended access protocol (EAP) provided continued MMB treatment to 138 patients following the completion of S1, S2 and earlier Phase 2 MMB studies. Of these, 105 remain on MMB with duration on therapy ranging up to 9.8 years.

RESULTS

A Significant Cohort of Patients with Myelofibrosis Have Received Extended MMB Therapy

Across these studies, more than 550 patients with MF have received MMB, with extended durability: 336 patients remained on MMB up to 9.8 years following MMB exposure.

MMB patients. Importantly, as noted in S1, patients who crossed-over from RUX to MMB for ET, maintained on MMB following RUX→MMB cross-over.

Other Safety Data

During the overall period of exposure in S1 and S2, MMB demonstrated low rates of AEs of interest for the JAKI class: catarracts [8] 6.8% in S1 and 3.5% in S2; non-melanoma skin cancers [3] 4.9% in S1 and 4.2% in S2; opportunistic infections [4] 1.0% in S1 and 0.7% in S2; and thrombosis [5] 3.2% in S1 and 7.0% in S2.

Peripheral neuropathy (PN) was notably infrequent, low grade, and often reversible across overall MMB exposure. In S1 and S2 overall, events of PN were "3%. Grade 1, 2, and on RUX were 2, 3.2% and 3.2% respectively. In S1, PN was reported for 9.3% of patients receiving MMB compared to 5.6% for RUX (Table 3A). Very few patients who received MMB at any time during S1 and S2 (8/411 patients in S1 and 3/144 in S2) did not receive or return to the original AE grade on study.

CONCLUSIONS

The further analyses of data from the S51 JAKI naïve and previously JAKI-treated patients with MF who received MMB at any time during the RT and ET phases of the Phase 3 SIMPLIFY studies presented here confirm the remarkable durability and long-term tolerability of MMB therapy, with 336 patients remaining on MMB for 4.8 weeks in 148 patients for ≥ 2 years.

In contrast to RUX, MMB therapy elicited sustained increases in Hgb and improved or maintained PLT counts in the RT periods of both studies, leading to low rates of hematologic AEs in the MMB patients. Importantly, as noted in S1, patients who crossed-over from RUX to MBB for ET, also received a rapid and sustained improvement in Hgb and PLT levels, despite prior RUX myelosuppression.

This lack of hematologic toxicity is associated with substantially higher dose intensity for MMB vs RUX as described in the companion poster #EP1113.

Overall, these findings are consistent with MMB’s differentiated pharmacological and clinical profile as an inhibitor of JAK1, JAK2 and ACRV1 which is associated with low myelosuppressive potential and consequent anaemia and thrombocytopenia benefits which contrast with the high myelosuppressive effect during RUX therapy.

Importantly, no new safety signals or cumulative toxicity were observed during extended MMB dosing.

Peripheral neuropathy was uncommon, of low grade, and not progressive.

These data demonstrate MMB’s potential ability to address the unmet needs of patients with intermediate/high risk MF.