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# TRANSFUSION INDEPENDENCE IS ASSOCIATED WITH IMPROVED OVERALL SURVIVAL IN MYELOFIBROSIS PATIENTS RECEIVING MOMELOTINIB

Topic: 16. Myeloproliferative neoplasms - Clinical

Keywords: Anemia, Janus Kinase inhibitor, Myelofibrosis, Survival

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**Background:** Momelotinib (MMB) is a potent JAK1, JAK2 and ACVR1 inhibitor with clinical activity against the hallmark features of myelofibrosis (MF), namely anemia, constitutional symptoms and splenomegaly, across the continuum of JAKi naïve or previously JAKi treated intermediate/high risk MF patients as demonstrated in the previously conducted Phase 3 SIMPLIFY-1 & -2 clinical trials (S1, S2). S1 enrolled JAKi-naïve patients with MF (n=432) double-blind randomized 1:1 to MMB or ruxolitinib (RUX). S2 enrolled patients with MF with hematological toxicity during prior RUX therapy (n=156) randomized 2:1 to open-label MMB or best available therapy (BAT; consisting of RUX in 88% of patients). In both trials, following the 24-week randomized treatment (RT) period, patients could continue MMB (MMB→MMB) and those randomized to RUX/BAT could cross-over to MMB (RUX/BAT→MMB) for extended treatment (ET).

Previously published data from the SIMPLIFY studies demonstrate robust overall survival (OS) for MMB-treated patients in S1 and S2 (median not reached and 34.3 months, respectively) with a maximum follow up of approximately 5 years and median of 2.9 years in S1 and 2.3 years in S2.

**Aims:** OS data for patients receiving MMB in S1 and S2 are reported here for subgroups defined by Week 24 (W24) transfusion independence (TI) responders vs non-responders, and also other efficacy endpoints.

**Methods:** Survival was estimated using KM analysis with descriptive log-rank tests for comparison applied (all p-values are descriptive).

**Results:** As previously reported, W24 TI rates were higher in the MMB arms of S1 (67% vs 49%) and S2 (43% vs 21%). In S1, W24 TI responders in the MMB group show an OS advantage, with median OS not reached and 3-year survival of 80% (HR=0.30; p<0.0001) compared to MMB TI non-responders. Similarly in S2, W24 TI responders in

the MMB group show a trend toward better OS compared to TI non-responders (HR=0.57; p=0.0652). The HRs in S1 for MMB responders vs non-responders for W24 SRR and TSS were 0.59 (p=0.0904) and 0.65 (p=0.1657), respectively. Alternative analyses using OS defined from W24 demonstrated consistent results.

**Summary/Conclusion:** These new analyses suggest JAKi naïve patients receiving MMB who maintain or achieve TI at W24 have favorable OS compared to MMB TI non-responders, with a similar trend observed in S2. These findings are consistent with anemia and transfusion dependency being key predictors of shortened OS in MF and suggest that TI response at W24 may become a surrogate for clinical benefit, supporting the clinical relevance of MMB's differentiated pro-erythropoietic ACVR1 inhibition.

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