

INVESTIGATE THE EFFECT OF MOMELOTINIB THROUGH HIGH RESOLUTION ULTRASOUND ASSESSMENT OF SPLEEN STIFFNESS AND DIMENSION MEASUREMENTS: A REAL-LIFE COMPARISON WITH PIVOTAL TRIALS

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Introduction: Momelotinib (MMB) is a JAK1/JAK2 and ACVR1 inhibitor recently approved for the treatment of myelofibrosis (MF), demonstrating efficacy in improving anemia, constitutional symptoms, and splenomegaly in the phase III SIMPLIFY-1, SIMPLIFY-2, and MOMENTUM trials. In those studies, spleen response was evaluated by MRI or CT scan, modalities not routinely available in all clinical settings. High resolution Ultrasound (HUS) is a widely accessible and non-invasive tool that may offer a practical alternative for spleen monitoring and stiffness assessment. We report a real-life experience on the evaluation of splenic response and stiffness changes in MF patients treated with MMB, comparing our findings with pivotal trial data.

Methods: We retrospectively analyzed 16 MF patients (11 PMF, 5 SMF) treated with MMB between 2023 and 2025 at a single Italian hematology center (AOUP). All patients met WHO 2008/2016 criteria for MF and received MMB according to clinical indications (median starting dose: 200 mg/day). Spleen size (length in cm and area in cm²) and stiffness (kPa) were assessed using shear wave elastography at baseline and after 6-18 months of treatment using standardized elastographic protocols. Clinical and hematologic responses were also collected. Data were compared with published outcomes from the SIMPLIFY1/2 and MOMENTUM trials.

Results: Median age at treatment start was 67 years (range

61-82); 12 patients (74%) were JAK2 V617F-mutated, 2 (13%) CALR-mutated, and 2 (13%) triple negative. Baseline median spleen length was 19.5 cm (range 15-26), and median stiffness was 98 kPa (range 31-176). After 6-18 months of MMB therapy, 9/16 patients (56%) achieved a $\geq 35\%$ reduction in spleen length by HUS, corresponding to the spleen response rate reported in SIMPLIFY-1 (42%) and MOMENTUM (39%) when measured by MRI/CT. Median spleen stiffness decreased from 98 kPa to 38 kPa, with a greater reduction observed in patients achieving spleen volume response. Hemoglobin levels improved in 11/16 patients (69%), consistent with the known erythropoietic effect of MMB, while transfusion dependence was reduced in 4/7 previously transfusion-dependent patients.

Conclusions: Our real-life data confirm that momelotinib induces significant spleen reduction and improvement in splenic stiffness, with response rates comparable to those reported in pivotal phase III trials, despite the use of HUS instead of MRI/CT. High resolution Ultrasound-based spleen evaluation, including elastographic stiffness measurement, represents a feasible, cost-effective, and reproducible method for monitoring treatment response in MF patients receiving JAK inhibitors. Larger multicenter studies are warranted to validate HUS-based assessment as a reliable surrogate for imaging endpoints in clinical trials and routine practice.