Phase III FREEDOM2 trial: Fedratinib in patients with myelofibrosis previously treated with ruxolitinib (NCT03952039)

N = 201

DESIGN (2:1 randomization)

Stratification at randomization according to:	**Spleen size** by palpation: <15 cm below LCM vs ≥15 cm below LCM **Platelets**: ≥50 to <100 x 10^9/L vs ≥100 x 10^9/L **R/R to RUX vs intolerant** to RUX

Fedratinib (n = 134)	**BAT* (n = 67)**
400 mg/day (4 × 100 mg capsules QD)	52 received RUX†
≤6 cycles; 28-day cycles until unacceptable toxicity, lack of therapeutic effect, PD, or withdrawal of consent	≤6 cycles

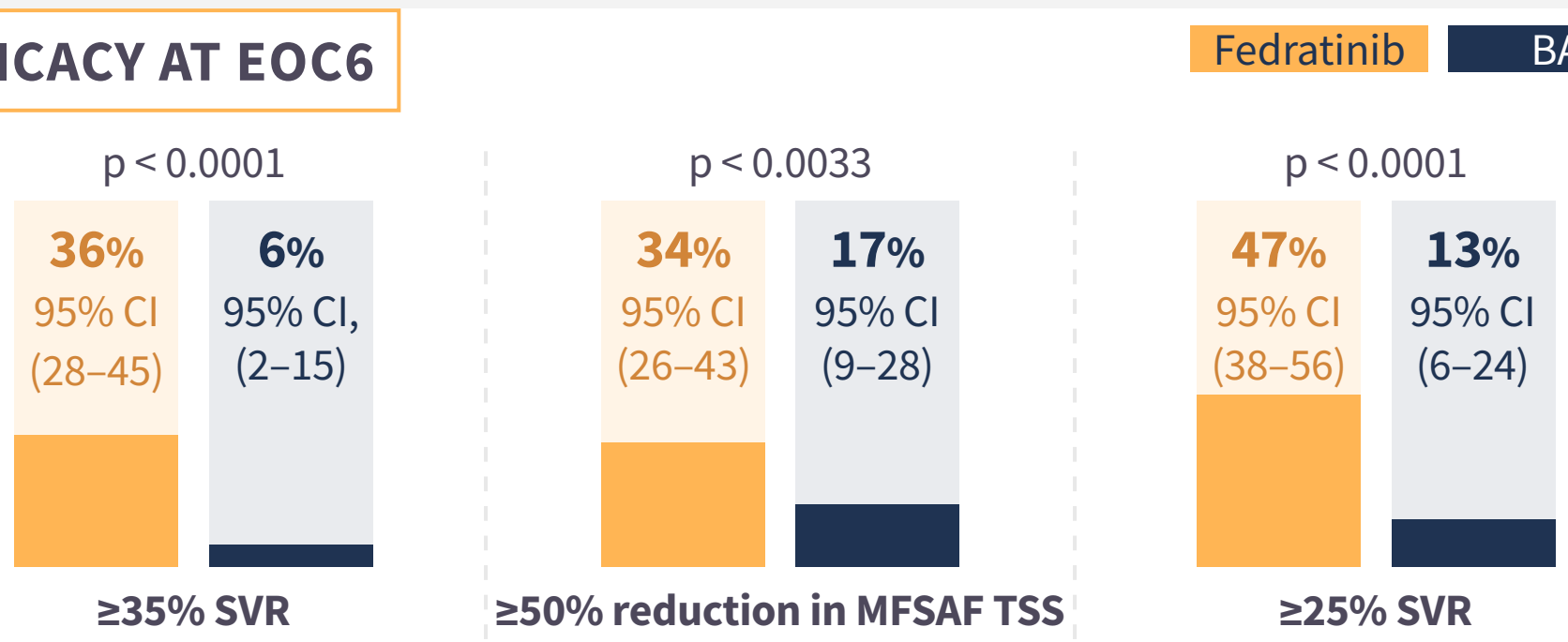
*Among the 67 patients, 78% received RUX, 28% received RBC transfusion, and 19% received HU. Other medications received included danazol, mercaptopurine, methylprednisolone, interferon, prednisone, prednisolone, and thalidomide. Crossover to fedratinib from BAT was permitted after Cycle 6 response assessment or at any time in the event of confirmed PD.

†Median initial daily dose was 20.0 mg and median maximum daily dose was 30.0 mg.

Primary endpoint: ≥35% SVR at EOC6
Key secondary endpoints: ≥50% reduction in MFSAF TSS at EOC6; ≥25% SVR at EOC6

Key eligibility: Aged ≥18 years; intermediate-2 or high-risk MF that was relapsed, refractory, or intolerant to RUX; ECOG PS 0–2

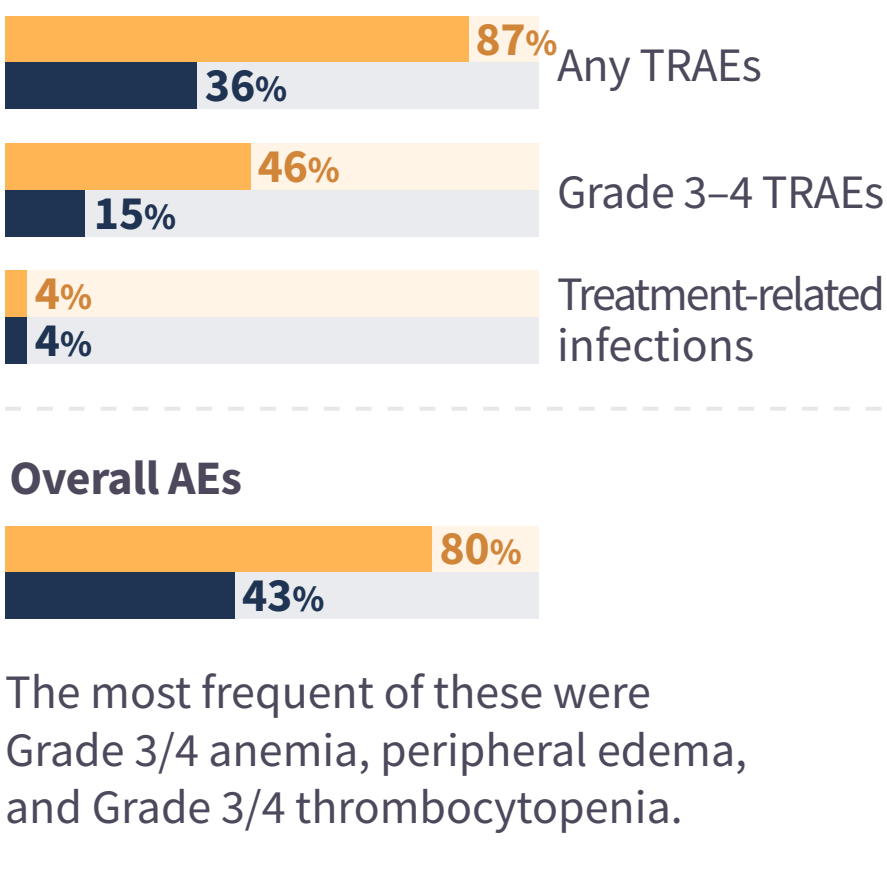
EFFICACY AT EOC6



The SVR35 benefit of fedratinib vs BAT was observed across all clinically relevant subgroups and was numerically higher in patients intolerant to RUX vs those R/R to RUX and in patients with a lower platelet count (≥50 to <100 × 10^9 platelets/L) at baseline.

SAFETY

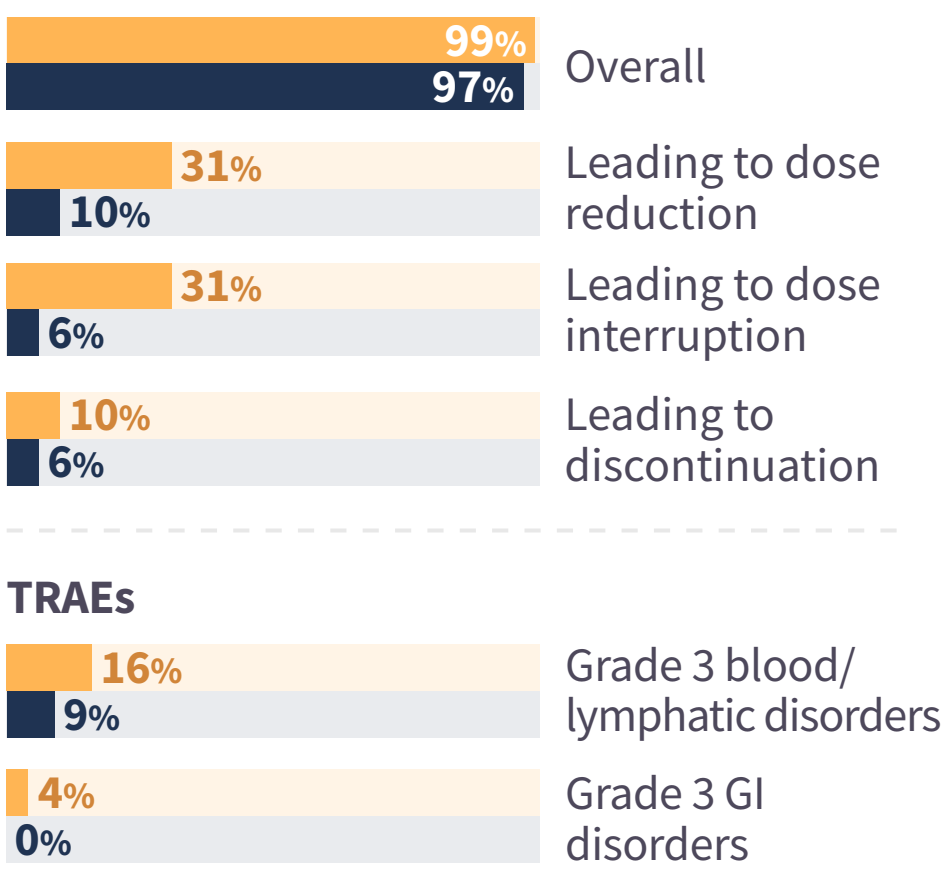
Entire treatment period



The most frequent of these were Grade 3/4 anemia, peripheral edema, and Grade 3/4 thrombocytopenia.

First six cycles

(to account for differences in exposure between groups)



Findings from FREEDOM2 demonstrate a clear efficacy benefit of fedratinib vs BAT and support fedratinib as a second-line JAKi option to reduce spleen volume after RUX failure or intolerance in patients with MF.

Abbreviations: BAT, best available therapy; EOC6, end of Cycle 6; ECOG PS, Eastern Cooperative Oncology Group performance status; HU, hydroxyurea; ITT, intention-to-treat; JAKi, Janus kinase inhibitor; LCM, left costal margin; MF, myelofibrosis; MSAF; Myelofibrosis Symptom Assessment Form; PD, progressive disease; R/R, relapsed/refractory; RBC, red blood cell; RUX, ruxolitinib; SVR, spleen volume reduction; SVR35, SVR of at least 35%; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; TSS, total symptom score; QD, once daily.

Harrison C, *et al. Lancet Haematol*. 2024;11(10):e729-e740.

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