A Phase II randomized dose-ranging study of the JAK2-selective inhibitor SAR302503 in patients with intermediate-2 or high-risk primary myelofibrosis (MF), post-polycythemia vera MF, or post-essential thrombocythemia MF

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Aims and methods: This multicenter, randomized, dose-ranging study in patients with intermediate-2 or high-risk MF included three escalating doses of SAR302503: 300 mg (n=10), 400 mg (n=10), and 500 mg (n=11). Patients had a spleen response if they had a ≥35% reduction in volume) in the highest dose group. The most common AEs across all doses were anemia and diarrhea. With PK exposure and pharmacodynamic (PD) results from an open-label Phase II study of three escalating doses of SAR302503 in patients with MF (ARD11936; NCT01420770).

Here, we report the efficacy, safety, and pharmacokinetic (PK) and pharmacodynamic (PD) results from an open-label Phase II study of three escalating doses of SAR302503 in patients with MF (ARD11936; NCT01420770).

Results occur at high frequency in MF, inducing hyperactivation of the JAK–STAT pathway.2 Janus kinase 2 (JAK2) and/or myeloproliferative leukemia (MPL) gene mutations V617F allele burden, with an acceptable safety profile.3,4 The median number of cycles was 17 among the three groups. In all dose groups, patients with constitutional symptoms at baseline reported improvement in ≥50% of symptoms by Cycle 3 (EOC3).

The most common AEs across all doses were anemia and diarrhea. With PK exposure and pharmacodynamic (PD) results from an open-label Phase II study of three escalating doses of SAR302503 in patients with MF (ARD11936; NCT01420770).

Conclusions

1. Patients with 3 cycles of SAR302503 were associated with clinically meaningful reductions in symptoms and improvements in constitutional symptoms without significant toxicity.

2. A spleen response rate was observed in 30.3% of patients across 300 mg–500 mg doses, with a ≥70% decrease in spleen volume.

3. Patients who did not respond to SAR302503 had a ≥70% reduction in spleen volume compared to baseline.

Additional Bibliography


References

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Disclosures

The authors declare no conflicts of interest.

There are no relevant conflicts of interest to disclose.

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Table 1. Baseline characteristics of the study population.

Table 2. Baseline characteristics of the study population.

Figure 1. Effect of SAR302503 on symptoms at EOC3.

Figure 2. Effect of SAR302503 on symptoms at EOC3.

Figure 3. Effect of SAR302503 on symptoms at EOC3.

Figure 4. Effect of SAR302503 on symptoms at EOC3.

Figure 5. Effect of SAR302503 on symptoms at EOC3.

Figure 6. Effect of SAR302503 on symptoms at EOC3.