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P1030 SPLEEN VOLUME REDUCTION PREDICTS SURVIVAL IN MYELOFIBROSIS PATIENTS ON PACRITINIB BUT NOT BEST AVAILABLE THERAPY: PERSIST-2 LANDMARK OVERALL SURVIVAL ANALYSIS

Topic: 16. Myeloproliferative neoplasms - Clinical

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Background:

Myelofibrosis is a life-limiting malignancy characterized by marrow fibrosis, splenomegaly, and progressive cytopenias. JAK2 inhibitors can reduce spleen volume, which is considered a surrogate for disease response. For example, ≥10% spleen volume reduction (SVR) on ruxolitinib (RUX) is associated with improved overall survival (OS) among patients with normal platelet counts (≥100×10^9/L). RUX cannot be administered at full dose in patients with moderate or severe thrombocytopenia, and it is not known whether the association between SVR and OS persists in such patients.

Pacritinib (PAC) is a JAK1-sparing inhibitor of JAK2/IRAK1/ACVR1 that demonstrated SVR benefit vs best available therapy (BAT; including RUX) in PERSIST-2, which enrolled myelofibrosis patients with platelet counts ≤100×10^9/L.

Aims:

To assess whether SVR is associated with OS in myelofibrosis patients with moderate and severe thrombocytopenia treated with PAC or with BAT (including RUX).

Methods:

This analysis includes patients enrolled in PERSIST-2 who were alive and on study at the start of the 12-week SVR assessment window (study week 10) and were treated with PAC 200 mg BID or BAT. Spleen volume was measured radiographically (MRI or CT). OS was evaluated among SVR responders vs non-responders within each treatment arm based on different SVR thresholds (≥35%, ≥20%, ≥10%, >0%) and a landmark analysis methodology. OS curves were compared using the log-rank test.

Results:

Among all analyzed thresholds, SVR≥10% had the greatest separation in OS between responders (n=65) and non-responders (n=24) for PAC, with no subsequent deaths among responders versus 5 among non-responders (HR=0.0 [95% CI: 0.0, 0.14], *P*<0.0001 [**Fig 1a**]). Both SVR>0% and SVR≥20% (**Fig 1b**) at week 12 were associated with improved survival, though separation of the responder vs non-responder curves was not as great. Interestingly, while SVR≥35% is considered to be the threshold for spleen response in myelofibrosis studies, this threshold was a less predictive indicator of survival on PAC (HR=0.0 [95% CI: 0.0, 2.71], *P*=0.3516), as many patients with SVR<35% were long-term survivors.

Counter to the experience with pacritinib, achieving SVR on BAT (n=84) was not associated with improved

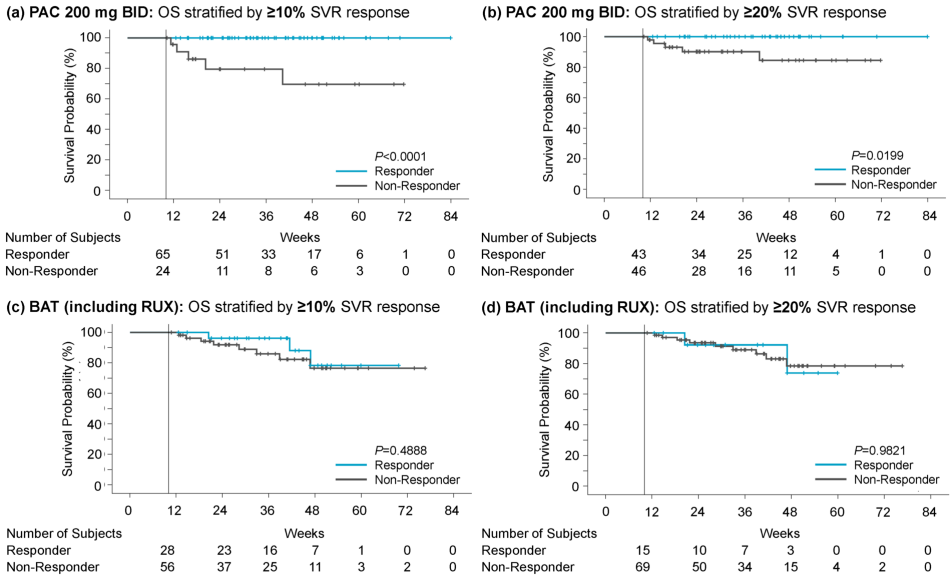
survival, irrespective of the SVR threshold. Neither SVR≥10% (**Fig 1c**) nor SVR≥20% (**Fig 1d**) predicted survival on the BAT arm (HR=0.63 [95% CI: 0.17, 2.37], *P*=0.4888 and HR=1.02 [95% CI:0.22, 4.72], *P*=0.9821, respectively).

Of the 28 patients on BAT who achieved SVR ≥10%, 23 (82%) were treated with RUX. Among these 23 patients, most were receiving low-dose RUX at the time of the landmark: 78% were on ≤10 mg BID and 43% were on ≤5 mg BID. By contrast, the median relative dose intensity on PAC was 100% (200 mg BID) through week 12 among both SVR ≥10% responders and non-responders.

Summary/Conclusion:

In myelofibrosis patients with moderate and severe thrombocytopenia, achieving ≥10% SVR on full-dose PAC was associated with significant OS benefit. By contrast, this association was not found with BAT, even though most responders were on RUX, albeit at low doses. As PAC can be given at full dose regardless of platelet count, it is possible that PAC may offer a unique survival advantage for myelofibrosis patients with moderate or severe thrombocytopenia who achieve spleen reduction.

Figure 1. Overall Survival for Responders vs Non-responders



Abbreviations: BAT, best available therapy; BID, twice daily; PAC, pacritinib; OS, overall survival; RUX, ruxolitinib; SVR, spleen volume response