PROGNOSTIC IMPACT OF EARLY SPLEEN RESPONSE IN PV PATIENTS TREATED WITH RUXOLITINIB: A REAL-WORLD COOPERATIVE STUDY

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Introduction

Ruxolitinib (RUX) is indicated for patients (pts) with Polycythemia Vera (PV) who are resistant or intolerant to hydroxyurea.[1,2]

Objectives

To investigate early predictors of long-term outcomes in this setting.

Methods

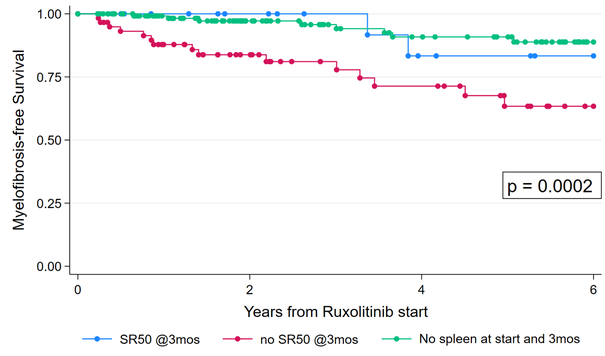
We performed a retrospective multicenter analysis on 218 PV patients treated with second-line ruxolitinib ("PV-ARC" study, NCT06134102). Spleen response (SR50: ≥50% reduction if spleen palpable ≥5cm; no palpable spleen if spleen palpable 1-5cm) and the complete hematological response (CHR: leukocytes <10×10^9/L, platelet <400×10^9/L, hematocrit <45% and no phlebotomy) at 3 months were evaluated and correlated with overall (OS), thrombosis-free (TFS), myelofibrosis-free (MFS) and event-free survival (EFS: including all 3 events) by Kaplan-Meier analysis with delayed entry.

Results

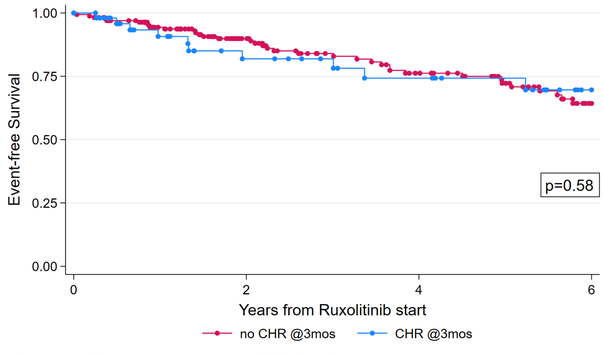
At ruxolitinib start, 113 patients (51.8%) had palpable splenomegaly (≥5 cm in 52 patients, 46%); 41.3% had hematocrit >45% and/or required phlebotomies; 46.3% had leukocytes ≥10×10^9/L; 47.4% had PLT ≥400×10^9/L; 61.9% of patients had itching (mean score: 6.0). Median RUX dose was 20mg/die. At 3 months, 53/113 (46.9%) and 51/218 (23.4%) evaluable patients achieved SR50 and CHR, respectively; 11 patients had a double response (CHR + SR50). 105 (48.2%) patients had no palpable spleen at baseline and at 3 months. After a mean ruxolitinib therapy of 3.4 years, 47 patients discontinued the treatment (18, died on treatment; 5, disease progression; 4, lack of SR; 3, thrombocytopenia; 8 anemia; 6, non-hematological toxicities; 3, ASCT). Seven patients had a thrombosis, 18 died (5, thrombo-hemorrhagic events; 6, 2nd neoplasms; 2, COVID-19 infections; 5, unknown), and 27 progressed to post-PV myelofibrosis/acute leukemia, for a 5-year TFS, OS, MFS and EFS of 96.6%, 92.1%, 82.4% and 73.3%, respectively.



5-year EFS was significantly longer in patients without baseline splenomegaly (86.1%). Patients achieving a SR50 had better EFS (74.0%) compared to non-responders (noSR50: 53.0%), with an HR (SR50 vs noSR50) of 0.47 (95% CI: 0.23–0.95, p=0.037) (global log-rank p=0.001). Analyzing individual events, no baseline splenomegaly and SR50 achievement were also significantly associated with improved 5-year MFS compared to non-responders (no splenomegaly: 94.5%, SR50: 83.6%, noSR50: 62.4%, global log-rank test p<0.001); HR (SR50 vs noSR50): 0.20, p<0.001).



Conversely, CHR was not associated with improved 5-year EFS (73.0% vs 74.3% in noCHR patients, p=0.58) and MFS (82.0% vs 82.5% in noCHR patients, p=0.52).



No differences in OS/TFS were observed by SR50/CHR /double response.

Discussion

Early SR50 is associated with long-term benefit in PV-patients receiving second-line ruxolitinib. Its evaluation may allow for earlier identification of patients with worse outcome and timely treatment decisions.

References

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