Abstract: P1050

Title: NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR) IN POLYCYTHEMIA VERA (PV): CORRELATION WITH ROPEG-INTERFERON RESPONSE IN LOW PV TRIAL

Abstract Type: Poster Presentation

Topic: Myeloproliferative neoplasms - Clinical

Background:

In PV, the JAK2V617F mutation activates circulating neutrophils, inducing chronic systemic inflammation. This leads to impaired function of T lymphocytes and natural killer (NK) cells, fostering immune dysfunction, clonal expansion, and immune evasion. The neutrophil-to-lymphocyte ratio (NLR) reflects this dual immune process, serving as a potential inflammatory biomarker for critical outcomes in PV. Interferon-alpha (IFN-alpha) therapy showed a significant favorable impact on lymphocyte subsets and neutrophil reduction compared to hydroxyurea in PV patients.

Aims:

To assess the impact of interferon therapy on inflammation in PV patients, we examined NLR levels in the Ropeg-interferon alpha-2b arm versus phlebotomy alone (Ph-O) in the phase II low-PV trial.

Methods:

In 126 patients, we analyzed (i) patient profiles based on NLR levels at randomization, (ii) NLR variations in the two arms at 12 and 24 months, and (iii) the correlation between NLR levels, patient response, and JAK2 V617F allele burden (NEJM Evid 2023).

Results:

i. Patients were stratified according to NLR < or > 3.5 (median value at baseline). Patients with NLR > 3.5 had a longer history of PV prior to enrolment (21.4 vs. 7.2 months; p=0.004), were more likely splenomegalic (41.5% vs. 20.0%; p=0.012) and had a higher *JAK2 V617F* VAF (56% vs. 20% p=0.001). Cases with NLR > 3.5 had laboratory tests confirming a more proliferative disease (higher leukocytes, LDH and bone marrow hipercellularity).

ii. In Ropeg patients a decrease in NLR levels was found; it occurred within the first 3 months and was mainly due to the decrease in neutrophils (60%) rather than lymphocytes (34%) (Fig 1). After 12 months, the difference between Ropeg and Phl-O in the % of subjects with NLR improvement (i.e. <3.5) was significant (68.3% vs. 43.9%, respectively, p=0.008). This trend was also substantially confirmed at 24 months in responders.

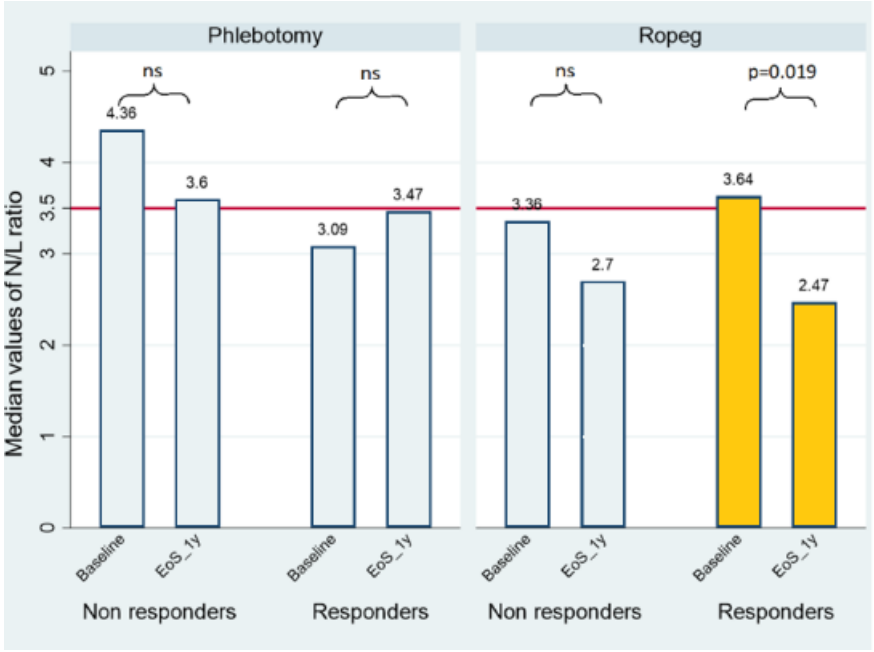
iii. By protocol, responders were defined as those who maintained HCT <45% in the first year, and were 81% vs. 51% for Ropeg vs. Phl-O, respectively. Phl-O non-responders had higher baseline NLR values and 6/8 of them met the definition of progressive disease. In contrast, NLR levels were <3.5 in Phl-O responders at baseline and after 12 months. In the Ropeg arm, both responders and non-responders had a decrease in NLR compared to baseline, but this drop was statistically significant at 12 months only in responders (p=0.019, Fig. 1). In this arm, the decrease in JAK2 VAF from baseline was found to be linearly associated with the decrease in NLR (beta=1.65, p=0.025) with a Pearson correlation coefficient (r) of 0.307. This association was more pronounced for the decrease in neutrophils (beta=1.72, p=0.016, r=0.323) than for the decrease in lymphocytes (beta=1.22, p=0.044, r=0.236). In the Phl-O arm, as expected, no changes between two markers at 12 months were found.

Summary/Conclusion:

In chemotherapy-naïve PV patients enrolled in the Low-PV trial, high NLR reflects hyper-inflammation, more

proliferative disease and is associated with higher VAF levels of JAK2-V617F. Ropeginterferon was able to significantly reduce the inflammatory biomarker NLR, indicating modulation of the immune response, which was associated with improved therapeutic efficacy.

Figure 1. Changes in NLR levels in Phlebotomy and Ropeginterferon arms according to response at 12 months. A significant NLR decrease was seen in Ropeginterferon responders



Keywords: Ropeg-Interferon, Inflammation, Polycythemia vera