FOSTAMATINIB IN POLYMORBID CARDIOVASCULAR PATIENTS: WHEN AND WHOM? A MONOCENTRIC REAL LIFE EXPERIENCE

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INTRODUCTION

Fostamatinib is a spleen tyrosine kinase (SYK) inhibitor used in the treatment of chronic immune thrombocytopenia (ITP) from the second line of therapy onward. Its mechanism of action (Fig.1), which involves blocking antibody-mediated platelet phagocytosis rather than supporting the thrombopoietin-dependent proliferative drive, makes it a strong therapeutic option not only for TPO-refractory patients but also for those with multiple comorbidities, where good clinical practice dictates avoiding thrombocytosis secondary to treatment.
This approach underscores the growing need for tailored therapy from earlier treatment lines, aimed at reducing polypharmacy exposure and minimizing the risk of developing multidrug refractoriness.
Here, we present our real-world experience with fostamatinib across diverse treatment settings.

DISCUSSION

No significant difference in response maintenance was observed between patients with multiple prior treatments and those who received fostamatinib earlier in their treatment history. However, TPO receptor agonist-naïve patients who received fostamatinib as a second- or third-line therapy demonstrated a better and slightly faster response (13 days); in one patient, a sustained complete response (CR) was achieved, allowing for treatment discontinuation.
Patients with a history of major cardiovascular events maintained a favorable safety profile, with no new episodes reported.

Table n.1

CV risk factors	Pts n.	Pts %
Arterial hypertension	11	50%
Diabetes	4	18
Cardiovascular diseases	4	18
Dyslipidemia	7	32
Obesity	3	14

Table n.2

Treatment lines	Pts n.	Pts %
TPO	18	82
RTX	11	50
CSA	3	14
MMF	3	14
AZT	3	14
Splenectomy	6	27

PATIENTS & METHODS

We analyzed 22 patients with ITP (5 male, 17 female) with a median age at diagnosis of 45 years (range: 12–87). Fourteen patients had cardiovascular comorbidities, including 5 patients with more than 2 risk factors and 3 with a history of thrombotic events (Table 1).
Patients had received a median of 3 prior therapy lines (range: 1–10) before starting fostamatinib; 82% had previously been treated with TPOra (Table 2). Only four patients were TPOra-naïve: of these, two were treated with fostamatinib post-rituximab, while two were treated in the second line. The median age at initiation of fostamatinib was 63.5 years (range: 24–87). The primary reasons for shifting to fostamatinib included loss of response or non-response to prior therapies (14 patients); in 4 patients, fostamatinib was chosen due to a history of thrombotic events (2 myocardial infarctions, 1 arteriopathy, and 1 venous thrombosis). The observed responses included 8 complete responses (CR), 4 partial responses (R), and 8 non-responders (NR), while two patients were not evaluable due to early discontinuation from reduced tolerance. Among these, 7 patients had received four or more previous therapy lines, with a median response duration of 73 days (range: 32–525); among patients with fewer than four prior therapies, the median response duration was 88 days (range: 9–98). The median time to response was 15 days (range: 9–98). Patients who were TPOra-naïve achieved partial or complete responses. No cardiovascular events were recorded during treatment. Overall, 13 patients remain on fostamatinib therapy.

CONCLUSION

Although based on a small sample size, our data provide interesting insights into the potential role of fostamatinib within the treatment decision-making algorithm. Its primary action in modulating platelet destruction suggests that it may be advantageous for earlier use in the ITP treatment pathway, particularly benefiting patients with multiple cardiovascular comorbidities.