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POSTER ABSTRACTS

311.DISORDERS OF PLATELET NUMBER OR FUNCTION: CLINICAL AND EPIDEMIOLOGICAL

Avatrombopag Plus Fostamatinib Combination Efficacy and Safety in Patients with Immune Thrombocytopenia

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INTRODUCTION

Avatrombopag (AVA) is a thrombopoietin receptor agonist (TPO-RA), approved for the treatment of immune thrombocytopenia (ITP), as second line in subjects with chronic ITP unresponsive to other treatments. Global response rate of AVA is 69% with a mean duration of 12.4 weeks in its pivotal study [1]. The combination of TPO-RA plus immunosuppressive/immunomodulatory drugs could optimize treatment results in ITP, addressing different pathophysiological pathways [2]. Among the most widely used immunomodulatory drugs in these circumstances are steroids, azathioprine and mycophenolate. Fostamatinib (FOS) is a splenic tyrosine kinase (SYK) inhibitor. FOS blocks the cascade of signals mediated by SYK after the activation of FcγRs, reducing macrophage activity, proliferation of B lymphocytes and production of antibodies [3].

We present the experience in the combined use of AVA with fostamatinib in non-responders to said TPO-RA, an experience not reported to date.

METHODS

Retrospective, multicenter, international, observational, non-interventional study in patients diagnosed of primary ITP who have received treatment with AVA and FOS in combination between August 2022 and June 2023. We included patients who have not reached platelets >30x10e9/L after at least two weeks of treatment with daily 40mg of AVA, and FOS was prescribed in combination in these circumstances. Epidemiological characteristics, type of ITP, previous treatments received, starting dose, response, concomitant ITP treatment and toxicity are collected. ITP definition and response criteria are based on Provan et al [4]: Response (R) as platelets 30-100x10e9/L and complete response (CR) as platelets > 100x10e9/L. Data are described in percentages for the categorical variables and in medians and ranges for the quantitative ones.

RESULTS

In the period of time evaluated, a total of 55 patients received treatment with AVA in Spain and Norway. The Norwegian data was acquired from the Norwegian ITP registry. In 16 of 55 patients (29%), there was no response after 2 or more weeks with AVA 280 mg weekly. In 6 of these patients, FOS was combined with AVA at a dose of 280mg weekly. Table 1 describes the characteristics of the 6 patients treated with the combination. Median time from initiation of AVA to combination with FOS was 14 days (Range: 14-21 days). The overall response of the combination was 100% (1 R, 5 CR). Median time to R was 25 days and to CR 31 days. Table 2 describes the characteristics of each patient's response. With a median follow-up from the start to last follow up of treatment in combination was 212 days (Range: 45-313 days), there was no relapse. Tapering of AVA and/or FOS was attempted in 5 patients by reducing the dose of FOS in 1 patient and the dose of AVA in 4. In patients 1 and 4, AVA was stopped, but this resulted in drop in the platelets counts. CR was achieved after reintroduction AVA in combination.

With regard to toxicity, in the 6 patients treated with the combination AVA plus FOS, only two adverse events were described, both non-serious. One case of headache encountered with the use of AVA, before the initiation of FOS. The other event, was WHO grade 2 liver toxicity attributed to AVA. Hypertransaminasaemia was resolved after the interruption of avatrombopag for 6 days and reduction of AVA from 140mg to 60mg weekly.

CONCLUSIONS

In subjects with a lack of response to thrombopoietin analogues, the combination with immunosuppressants is an alternative to consider. The combination of avatrombopag and fostamatinib has been shown to be effective and safe, although longer series are needed to support these data.

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Table 1. Patients Characteristics

Patient	Sex	Age (years)	Phase of ITP	Lines of treatment before AVA	Treated with TPO-RA before AVA	Treated with ELT	Treated with ROM
1	Women	22	Chronic	4	No	No	No
2	Man	28	Persistent	5	Yes	No	No
3	Women	24	Chronic	4	Yes	Yes, R	Yes, CR*
4	Man	66	Chronic	4	Yes	No	Yes, CR**
5	Man	58	Chronic	5	Yes	No	No
6	Man	60	Chronic	5	Yes	Yes, R***	Yes, R***

*Stop ROM, because of platelets picks difficult to control; **Stop ROM, for patient convenience; ***Platelets between 30-40x10e9/L, despite high doses of TPO-RA so patient decided to change to a different treatment option.

AVA: Avatrombopag; CR: Complete Response; ELT: Eltrombopag; R: Response; ROM: Romiplostin

Table 2. Patients' response to avatrombopag and fostamatinib in combination.

Patient	Initial weekly dose of FOS * (mg)	Type of Response	Time from combination to platelets>30x10^9/L (days)	Time from combination to platelets>100x10^9/L (days)	Follow up since combination start (days)	Last weekly dose of FOS (mg)	Last weekly dose of AVA (mg)	Platelet count in last visit (x10^9/L)
1	1400	CR	3	5	45	1400	60	383
2	2100	CR	42	112	313	2100	280	145
3	1400	CR	4	4	232	1400	60	160
4	2100	CR	24	31	159	700	60	102
5	2100	R	26	NCR	277	2100	280	44
6	2100	CR	32	153	192	2100	140	129

AVA: Avatrombopag; FOS: Fostamatinib; NCR: Non complete response

*AVA dose was 280mg at the beginning in all cases.

Figure 1

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