UPDATE ON ITP PATIENTS TREATED WITH AVATROMBOPAG: A REAL-LIFE MONOCENTRIC EXPERIENCE

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Introduction

Thrombopoietin receptor agonists (TPO mimetics or TPO-RAs) represent the second-line therapy for the treatment of idiopathic thrombocytopenic purpura (ITP). Avatrombopag is a second-generation TPO mimetic that can be initiated in patients in the chronic phase of ITP. The mechanism of action of TPO mimetics involves binding to the thrombopoietin receptor, which triggers the activation of various signal transduction pathways and other pathways involved in anti-apoptotic mechanisms; this results in an increased platelet production. Various studies on Avatrombopag have demonstrated its efficacy and safety; in approximately 66% of patients, a platelet count of >50.000/µL was achieved by the eighth day of treatment, and an adequate response was also observed in those who had previously taken Romiplostim and/or Eltrombopag.[1] From the phase 2 study, the following adverse events (AEs/SAEs) were observed: headache, asthenia, mucocutaneous hemorrhagic manifestations, arthralgia, and diarrhea, none of which required major interventions. Thromboembolic events occurred in 11 patients (7%) under treatment, some of whom presented a platelet increase above 450.000/µL.[2] Four of these patients had thromboembolic risk factors with platelet values fluctuating between 39.000-271.000/µL.[3] Avatrombopag has the benefit of being taken independently of food and does not cause alterations in liver function.[2]

Aim

The aim of the study was to evaluate the efficacy and duration of treatment with avatrombopag in a group of patients with ITP followed at our center.

Materials and methods

We conducted a retrospective observational study on a monocentric cohort of 21 patients (Table 1).
The initial dosage of avatrombopag was 20 mg/day.
The median pre-treatment platelet count was 34.000/µL (1.000-146.000/µL).
Peripheral venous blood samples were collected weekly during the first month of treatment, and then at varying intervals based on the platelet count trend.
Data were collected between August 2022 and April 2024.
All patients were treated at our institution (AOU Careggi, Florence, Italy).

Table 1: Patient characteristics.

Patients, nr. pz (%)	**21 (100%)**
Gender, nr. pz (%)	
Female	15 (71%)
Male	6 (29%)
Median age, years (range) • <50 years • >50 years	55 (24-84) 9 (43%) 12 (57%)
Platelet value at ITP beginning, median (µL) (range)	12000 (2-78000)
Platelet value pre-avatrombopag, median (µL) (range)	34000 (1-146000)
Median of prevoious therapheutic lines, nr. (range)	3 (1-9)

Results

- After one week of treatment, the median platelet count was 89.000/µL (1.000-1.000.000/µL). The median time to achieve platelet values higher than baseline was 7 days (5-21).
- Three patients (14%) never reached a platelet count >50.000/µL.
- At the one-month follow-up, it was necessary to increase the dosage to 40 mg/day for 4 patients (19%).
- One month after starting avatrombopag treatment, 5 patients (24%) were on steroid therapy.
- Sixteen patients (79%) switched from a first-generation TPO mimetic to avatrombopag for the following reasons: 7 pts (43%) loss of response, 3 pts (19%) lack of response, 3 pts (19%) patient choice, 3 pts (19%) adverse events (1 patient with fluctuating platelet values, 2 patients with elevated transaminases).
- After one month of treatment, no statistically significant differences in response (PLT >50,000/µL) were observed between:
  - •Patients over or under 50 years old (p=0.67)
  - •Patients treated with more than or equal to/less than 3 > o ≤ 3 previous therapies (p=0.6)
  - •Male and female patients (p=0.33)
- No differences were found between those who had a platelet count below or above 15.000/µL at the start of treatment (p=1) or below or above 30.000/µL (p=0.38).
- Treatment was discontinued in 8 patients (38%) for various reasons:
  - •6 patients (24%) lack of response
  - •1 patient (5%) platelet count fluctuations
  - •1 patient (5%) adverse event
- Three patients (14%) temporarily suspended therapy due to thrombocytosis.
- Currently, 13 patients (62%) are on avatrombopag treatment, 8 of whom are on a dose lower than 20 mg/day. The median number of tablets taken weekly is 4 (2-21).
- The median treatment duration was 314 days (30-621).
- One patient (5%) died due to causes unrelated to the treatment.

Conclusions

Our analysis highlighted the efficacy of avatrombopag treatment, showing a durable response despite the number of previous therapies, including treatment with first-generation TPO mimetics. More than half of the patients are currently taking the drug with a good response and tolerance.

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