



Tirosin-chinasi e ITP:
nuove strategie
terapeutiche

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Esperienza sul sequencing terapeutico nel paziente con ITP refrattaria

Elena Rossi

Ematologia

Fondazione Policlinico A. Gemelli IRCCS

Università Cattolica, Roma

REFRACTORINESS

Table 4. Refractory ITP

Definition (all should be met)

- Failure to achieve at least R or loss of R after splenectomy*
- Need of treatment(s) (including, but not limited to, low dose of corticosteroids) to minimize the risk of clinically significant bleeding.† Need of on-demand or adjunctive therapy alone does not qualify the patient as refractory.
- Primary ITP confirmed by excluding other supervened causes of thrombocytopenia

Definition of on-demand therapy

- Any therapy used to temporarily increase the platelet count sufficiently to safely perform invasive procedures or in case of major bleeding or trauma‡

Definition of adjunctive therapy

- Any non-ITP specific therapy that may decrease bleeding (eg, antifibrinolytic agents, hormonal agents, DDAVP, recombinant factor VIIa, fibrin sealants). Platelet transfusion is also included.

Definition of response to therapy in refractory ITP

- Ability to maintain a platelet count sufficient to prevent clinically significant bleeding†§
- Ability to decrease toxic therapy (eg, corticosteroids) does not qualify for response but should be reported

Definition of response to on-demand therapy

- Control of bleeding in the specific situation
- Achievement of a platelet count sufficient to perform procedure or minimize bleeding from trauma

It was felt that ITP in adults cannot truly be called refractory before splenectomy is attempted.

REFRACTORINESS

TABLE 1 Overview of definitions of ‘refractory ITP’ in adults.

Author, year	Definition
Rodeghiero et al., 2009 ¹	Failed splenectomy or relapsed after splenectomy Bleeding symptoms or risk of bleeding requiring treatment Refractory patients may have temporary responses to corticosteroids or intravenous immunoglobulin (IVIG)
Neunert et al., 2011 ⁹	Bleeding that requires treatment occurring after splenectomy. Refractory patients may respond temporarily to corticosteroids or IVIG. Other causes of thrombocytopenia must be excluded by a thorough clinical evaluation
Cuker et al., 2016 ¹⁰	Bleeding risk that requires treatment occurring in patients after splenectomy or in patients who are unable or unwilling to undergo splenectomy
Provan et al., 2019 ⁷	Avoided a definition of refractory since many patients will eventually attain a haemostatically effective platelet count without splenectomy
Miltiadows et al., 2020 ¹¹	Lack of a platelet count response to at least two treatments (e.g. TPO-RAs and rituximab), no single medication that raises platelet count and bleeding
Vianelli et al., 2022 ¹²	Persistently low platelet counts despite all conventional therapies deemed safe for the specific patient, regardless of bleeding manifestations. The threshold value to identify ‘low’ platelet count is variable depending on the patient’s age, comorbidities and concomitant therapies (e.g. anti-platelet or anti-coagulant agents)

Abbreviations: ITP, immune thrombocytopenia; IWG, International Working Group; TPO-RAs, thrombopoietin receptor agonists.

IS SPLENECTOMY EFFECTIVE IN REFRACTORY ITP?

TABLE 1

Characteristic of patients who underwent splenectomy over time

	Overall (n = 185)	2011–2013 (n = 55)	2014–2016 (n = 63)	2017–2020 (n = 67)	p
Age at ITP diagnosis, years (median [IQR])	37.78 [23.23, 58.80]	39.03 [25.19, 61.23]	31.82 [22.41, 52.10]	37.72 [24.82, 61.08]	.338
Age at splenectomy, years (median [IQR])	43.28 [27.57, 64.35]	50.35 [26.58, 65.68]	40.01 [25.34, 60.42]	45.78 [31.35, 64.24]	.401
Male sex, n (%)	85 (45.9)	30 (54.5)	26 (41.3)	29 (43.3)	.304
Time between diagnosis and SPC, months (median [IQR])	24.59 [14.14, 71.27]	23.54 [13.97, 68.20]	21.63 [14.56, 74.08]	31.36 [15.30, 82.20]	.669
Phase of ITP at the time of splenectomy, n (%):					.759
Chronic	150 (81.1)	43 (78.2)	50 (79.4)	57 (85.1)	
Persistent	33 (17.8)	11 (20.0)	12 (19.0)	10 (14.9)	
Newly diagnosed	2 (1.1)	1 (1.8)	1 (1.6)	0 (0.0)	
Lines of ITP treatment received before splenectomy, n (%) ^a					.001
1–2	38 (20.5)	12 (21.8)	14 (22.2)	12 (17.9)	
3–4	66 (35.7)	29 (52.7)	24 (38.1)	13 (19.4)	
5–6	69 (37.3)	12 (21.8)	24 (38.1)	33 (49.3)	
>6	12 (6.5)	2 (3.6)	1 (1.6)	9 (13.4)	
Type of treatment received prior to splenectomy, n (%):					
IVIg	152 (82.2)	43 (78.2)	52 (82.5)	57 (85.1)	.610
Vinblastine	25 (13.7)	9 (16.4)	8 (12.9)	8 (12.3)	.791
Eltrombopag	75 (40.5)	14 (25.5)	21 (33.3)	40 (59.7)	<.001
Romiplostim	72 (38.9)	11 (20.0)	22 (34.9)	39 (58.2)	<.001
Eltrombopag or romiplostim	100 (54.1)	17 (30.9)	33 (52.4)	50 (74.6)	<.001
Rituximab	135 (73.0)	37 (67.3)	47 (74.6)	51 (76.1)	.515
Dapsone	79 (42.7)	16 (29.1)	22 (34.9)	41 (61.2)	.001
Immunosuppressive drugs ^b	23 (12.4)	6 (10.9)	4 (6.3)	13 (19.4)	.072

Abbreviations: IQR, interquartile range; ITP, immune thrombocytopenia; IVIg, intravenous immunoglobulin; SPC, splenectomy.
^aCorticosteroids and IVIg are considered one unique treatment line.
^bExcept rituximab.

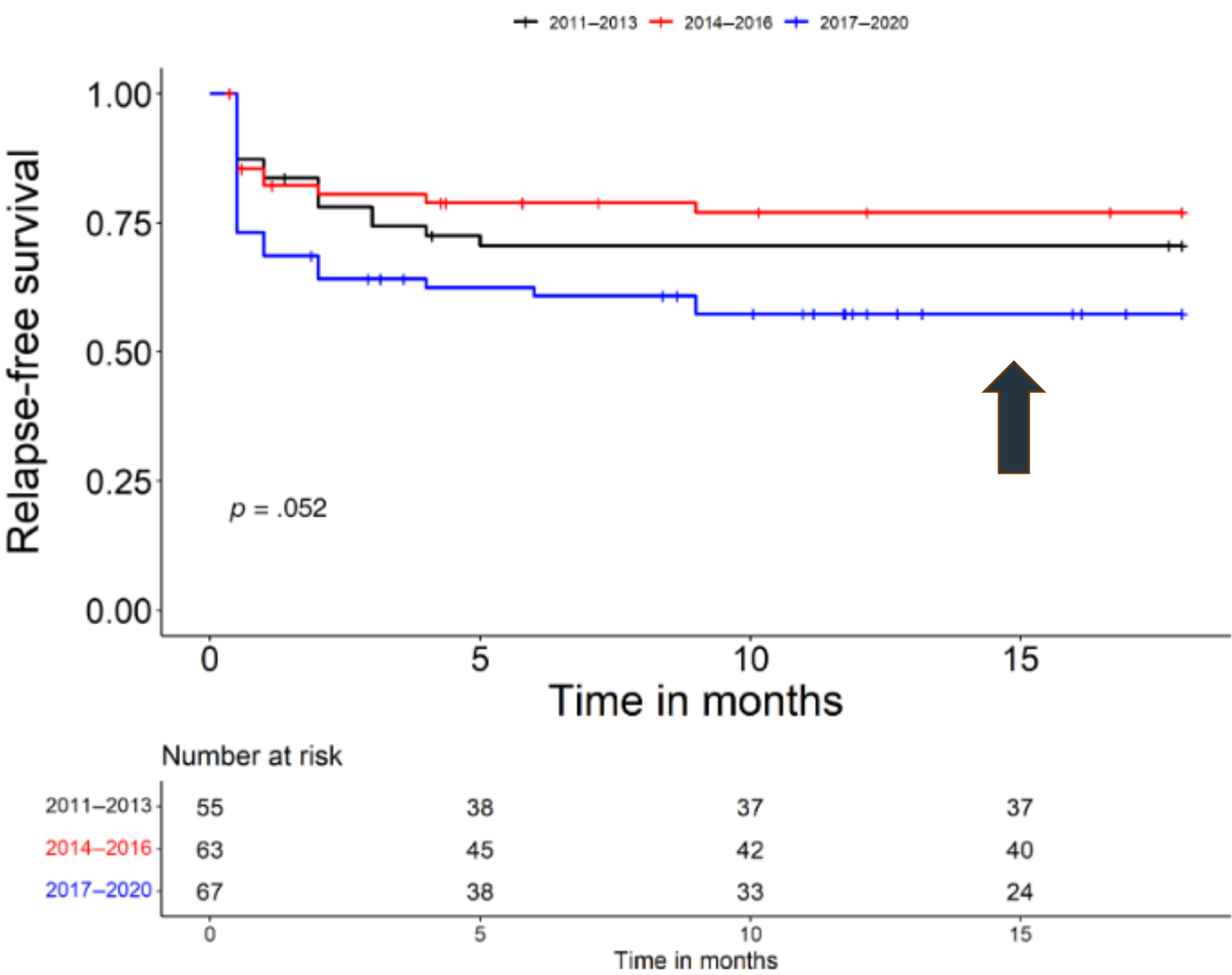


FIGURE 1 Kaplan–Meier analysis of relapse-free survival by time of splenectomy [Color figure can be viewed at wileyonlinelibrary.com]

Oggi i pazienti che vanno a splenectomia sono più trattati e con storia più lunga di malattia

IS SPLENECTOMY EFFECTIVE IN REFRACTORY ITP?

ITP refractory patients



Refractory: failed to respond to anti CD20 and available TPO-RAs (romiplostim, eltrombopag, avatrombopag...)

Is splenectomy indicated?

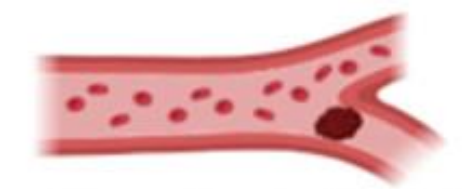
- CONS**
- Better knowledge of complications
 - Absence of robust predictive factors of sustained response

PRO

Splenectomy remains effective in multirefractory patients

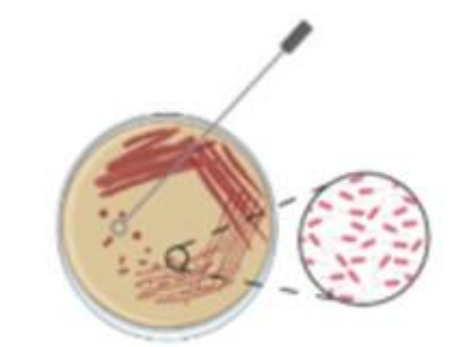
Particular situations:

- **Secondary ITP** (SLE, APS, CVID, CLL)
- **Elderly**



Thrombosis (mainly DVT and PE)

Risk of thrombosis?

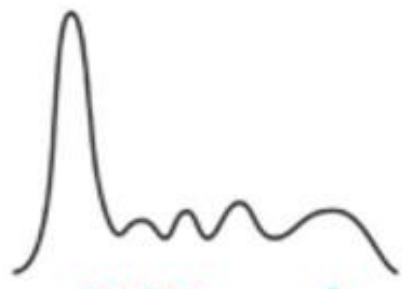


Severe bacterial infection including OPSI)

Risk of infection?



SLE and APS

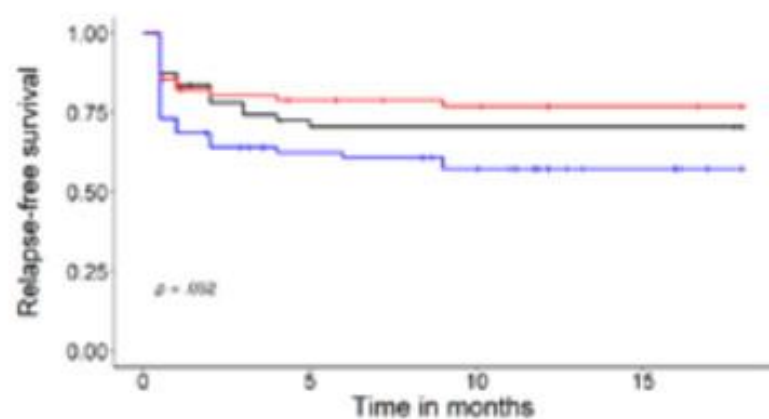


CVID and CLL



elderly

Splenectomy not strictly contraindicated. Depends on comorbidities



From Mageau et al, Am J Hematol 2022; 97: 10-17

REFRACTORINESS

Persistence of **severe** thrombocytopenia (platelets $<20 \times 10^9/L$) and **bleeding** in a patient with ITP who has received rituximab, two different TPO-RAs, and at least one immune suppressant medication and who does not respond or only briefly responds to high-dose corticosteroids or high-dose IVIG (less than 7 days).

Alternatively, qualifiers to the term refractory can be added to indicate the treatments to which the patient is refractory (e.g. ITP refractory to TPO-RA; ITP refractory to rituximab, TPO-RA and splenectomy)

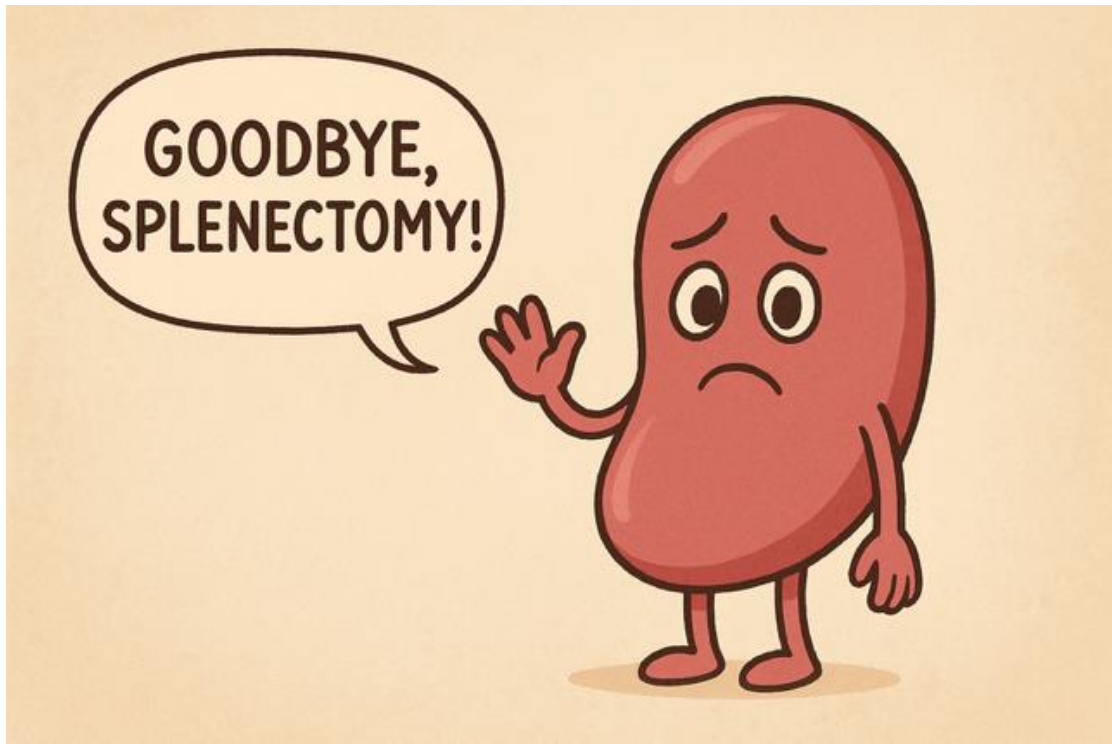


TABLE 2 Frequency of exposure of ITP patients to multiple lines of treatment—Preliminary output from the McMaster and Norwegian ITP Registries.

Patient group	McMaster ITP registry	Norwegian ITP registry
ITP patients in the Registry	N=531 including primary (n=408) and secondary ITP (n=123)	N=255 including primary (n=236) and secondary ITP (n=19)
First-line therapy ^a + any second-line ^b therapy	225 (42%)	116 (45.5%)
First-line therapy + rituximab + TPO-RA	40 (7.5%)	28 (11%)
First-line therapy + rituximab + TPO-RA + splenectomy	25 (4.7%)	8 (3.1%)
First-line therapy + rituximab + TPO-RA + any immune suppressant medication ^c	30 (5.6%)	4 (1.6%)
First-line therapy + rituximab + TPO-RA + any immune suppressant medication + splenectomy	20 (3.8%)	1 (0.4%)

The Patient Burden of Refractory Immune Thrombocytopenia

↓ **quality of life**

treatment side effect

disease anxiety
pregnancy fear

↑ **fatigue**



Table 5. Mortality risk of patients with thrombocytopenia, relative to the general population

Characteristics	Relative risk (95% CI)
Diagnosis	
Initial diagnosis of ITP (n = 150*)	1.5 (1.1-2.2)
ITP (n = 138)	1.3 (0.9-2.0)
Reclassified as secondary TP (n = 12)	6.0 (2.5-15.0)
Presenting symptoms	
Severe thrombocytopenia (n = 122)	1.5 (1.0-2.2)
Moderate thrombocytopenia (n = 28)	1.9 (0.8-4.5)
Hemorrhagic symptoms (n = 128)	1.5 (1.1-2.2)
No hemorrhagic symptoms (n = 22)	1.7 (0.4-6.8)
ITP depending on response to therapy†	
Complete response (n = 90)	0.7 (0.4-1.3)
Partial response (n = 24)	1.8 (0.6-5.5)
Response to maintenance therapy (n = 8)	1.8 (0.6-5.5)
No response (n = 12)	4.2 (1.7-10.0)
Referral	
Primary (n = 73)	1.9 (1.1-3.0)
Secondary (n = 77)	1.3 (0.7-2.2)

Mortality risks were estimated using the mortality rate ratio standardized for age, sex, and calendar time.

*Two patients were lost to follow-up.

†Response to therapy after 2 years of follow-up.

Table 4. Hospital admissions during long-term follow-up of patients with ITP

	ITP-related admissions		Unrelated admissions	
	No.	Incidence per 1000 person-years	No.	Incidence per 1000 person-years
Response at 2 years				
Complete response (n = 86)	39	53	54	73
Partial response (n = 23)	5	27	30	159
Response to maintenance therapy (n = 8)	10	153	14	214
No response (n = 11)	17	183	12	129
All	71	66	110	102

Long-term follow-up started 2 years after the initial diagnosis. Data are missing for 6 of the 134 patients with ITP.

First-line
therapeutic
options

Corticosteroids
Predniso(lo)ne/dexamethasone

IVIg*

Second-line
therapeutic
options

TPO-RA

TPO-RA

Rituximab**

Shared
decision

Fostamatinib^

Splenectomy§

Investigational
products and
combination
therapies #

Third-line
therapeutic
options and
beyond

Splenectomy

Combination therapy

TPO-RA

+

Immuno-
modulator
MMF,
fostamatinib,
cyclosporine

Monotherapies

MMF, cyclosporine,
sirolimus,
dapsonel, danazoll,
decitabine, etc

REFRACTORINESS PROBABILITY

splenectomy

- Older age
- Multiple previous lines of treatment
- Absence of previous response to corticosteroids and IVIg (debated)
- Low peak of platelet count after splenectomy
- Hepatic/mixed platelet sequestration on Indium-labeled autologous platelet study

rituximab

- Older age and male sex ? (debated)
- Chronic ITP (one study)
- Absence of previous response to corticosteroids (one registry)
- Absence of antinuclear antibodies (one study)

TPORAs

- Chronic ITP (debated)
- Previous splenectomy (debated)
- High TPO level in serum (debated)

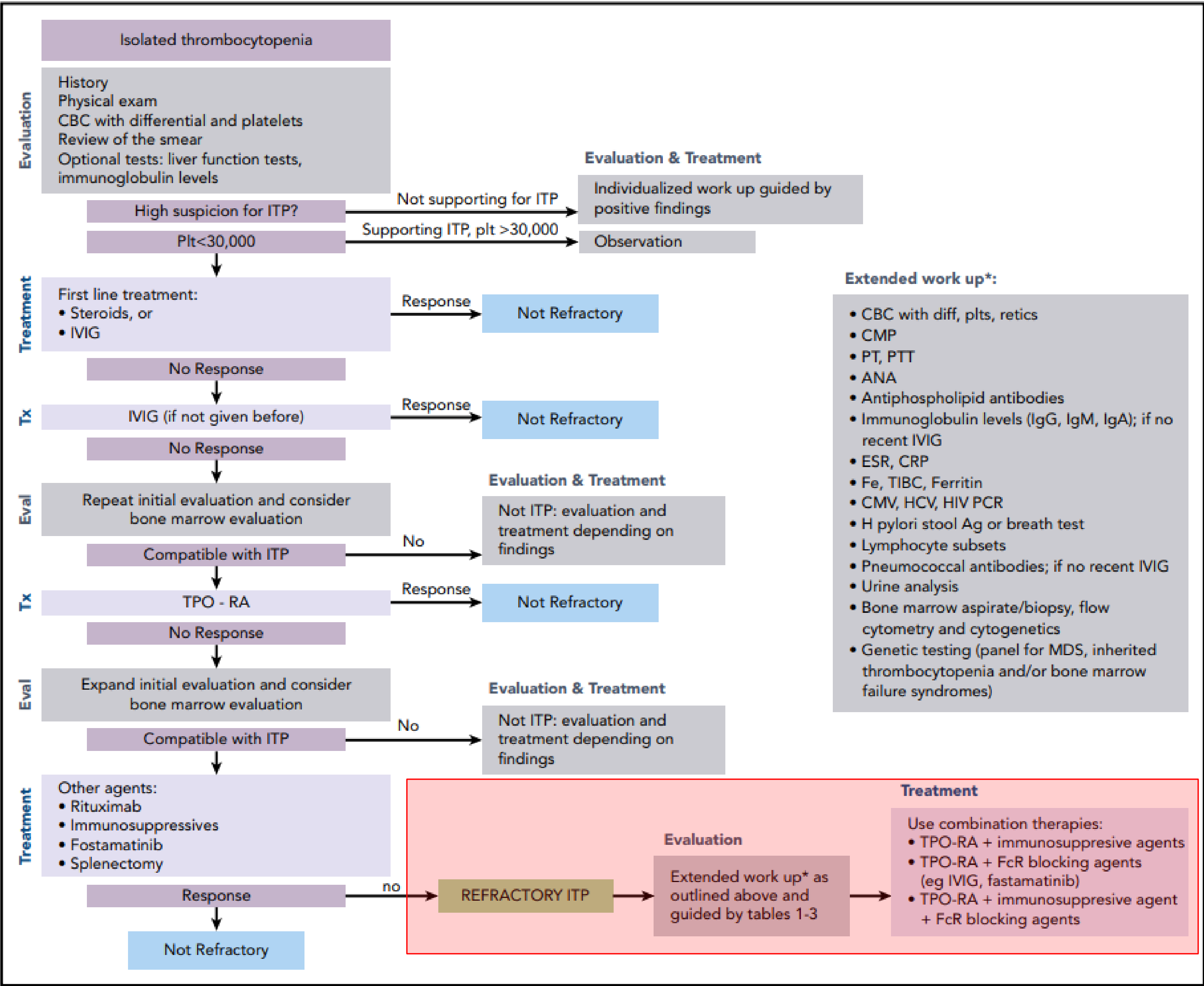
fostamatinib

- Used as >2nd line of treatment ? (one study)

multirefractory

- Bleeding at ITP diagnosis
- Absence of response to corticosteroids (one study)

Ma è una ITP primitiva?



Refractory Patients

There is no clear recommendation about how those refractory patient treatments should be managed.

Combined therapies are usually more effective than monotherapy in refractory patients. Ideally, agents with different mechanisms of action should be combined. Rescues have been described using steroids concomitantly with rituximab or TPO-RA.

In the event of no response to one treatment, **adding a new therapy concomitantly** may be better than suspending the former and starting with the new one only.

Other diagnoses, such as drug-induced thrombocytopenia, myelodysplastic syndrome or hereditary thrombocytopenia, should be considered in multirefractory patients.

The use of immunosuppressants, immunomodulators or cytostatic agents can be considered. Nevertheless, their side effects, especially those linked to an increased infection risk, make it advisable to balance carefully the benefit/risk ratio

COMBINATION TREATMENTS IN REFRACTORY PATIENTS

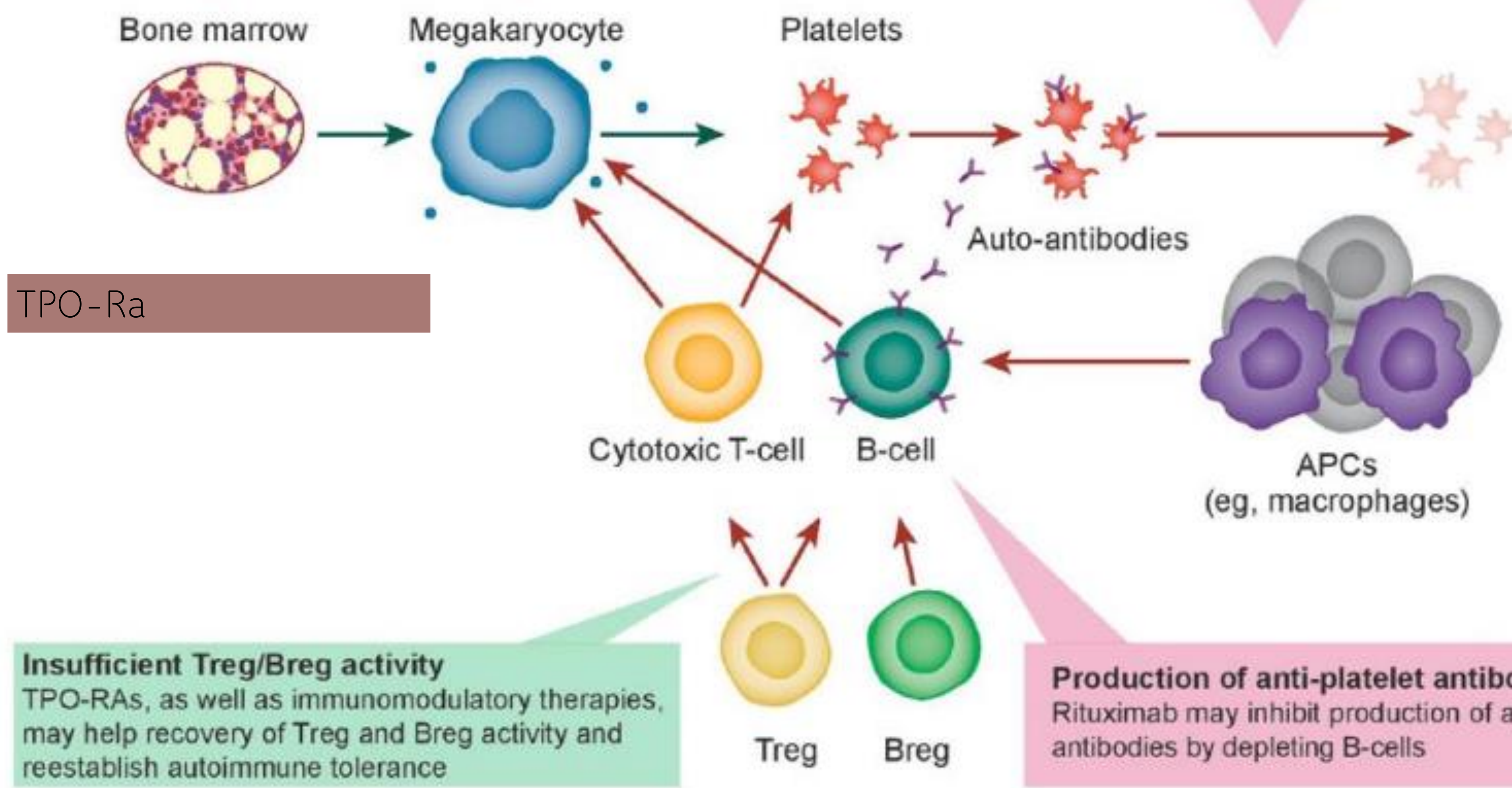
In a historical cohort of 400 ITP patients, 109 of the 234 treated received a combination therapy including PDN. The results showed a 50% response rate; however, the optimal treatment combination could not be identified, likely due to the retrospective nature of the study and the considerable variability in the treatment regimens

Table 2. Results of continuous treatments in patients with ITP during observation at our institution (n = 234).

Therapy	Patients (n)		Response			Non-R	Total ARs	Treatment time in months (mean/range)
	Total	Documented	Total R	Intolerability/R	SR/R			
Pred	92	88	64 (73%)	12/64	8/64	24 (27%)	30 (34%)	21.2 / 1–210
Aza	14	12	7 (58%)	1/7	1/7	5 (42%)	4 (33%)	13.6/0.5–48
Aza + Pred	82	78	42 (54%)	19/42	1/42	36 (46%)	34 (44%)	15/0.5–108
Romip (+Pred ^a)	52	45	35 (78%)	8/35	-	10 (22%)	15 (33%)	12,1/0.75–72
Eltromb	64	63	45 (71%)	14/45	4/45	18 (29%)	22 (35%)	15.6/0.5–96
MTX (+Pred ^b)	5	5	2 (40%)	-	-	3 (60%)	-	48.2/2–175
Cycl (+Pred ^c)	6	6	4 (66%)	-	-	2 (33%)	2 (33%)	13.3/1.5–29
Ciclo (+Pred ^d)	12	10	1 (10%)	-	-	9 (90%)	1 (10%)	5.8/0.75–18
MMF (+Pred ^e)	15	14	7 (50%)	3/7	-	7 (50%)	6 (43%)	15.7/ 1–60
Dapsone	3	3	1 (33%)	-	-	2 (66%)	-	41.3/ 2–120

Insufficient platelet production
Reduced platelet production or the lack of compensatory boost in platelet production can be addressed by TPO-RAs

Increased platelet destruction
Antibody-coated platelets are destroyed through opsonization primarily by macrophages. First-line ITP treatments, including corticosteroids and IVIG, reduce opsonization and subsequent antigen presentation that may lead to sustained autoimmune response



TPO-Ra

RITUXIMAB

Insufficient Treg/Breg activity
TPO-RAs, as well as immunomodulatory therapies, may help recovery of Treg and Breg activity and reestablish autoimmune tolerance

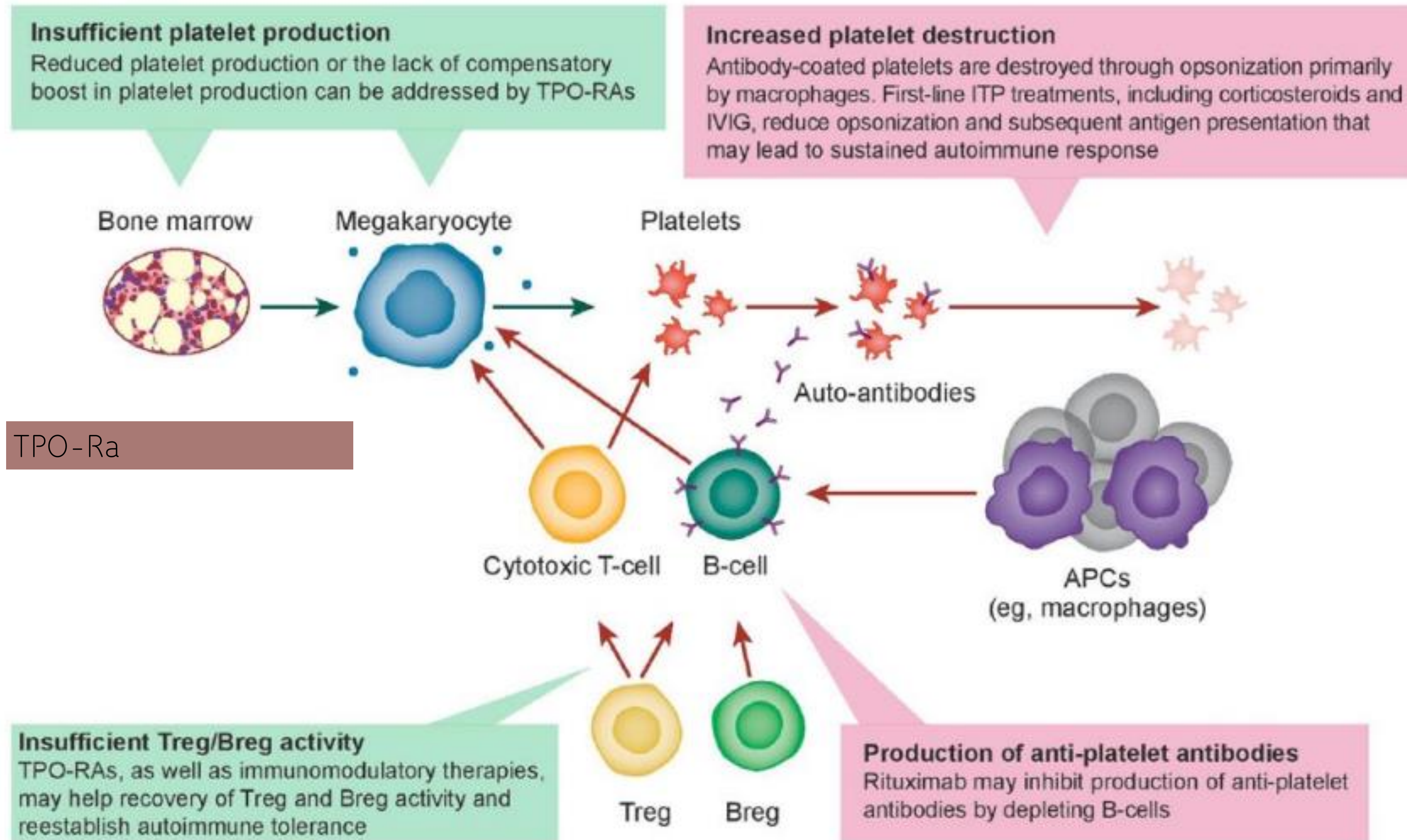
Production of anti-platelet antibodies
Rituximab may inhibit production of anti-platelet antibodies by depleting B-cells

Table 1 Characteristics of the study cohort (n = 8)

Analyzed trait	Statistical parameter ^a	
	n M (SD)	% Me (Q ₁ –Q ₃)
Gender		
Female	3	37.5
Male	5	62.5
Age before treatment line (year)	44.0 (17.2)	38.0 (32.0–52.0)
Age at ITP diagnosis (year)	32.6 (21.6)	31.0 (23.5–45.5)
ITP duration (month)	98.4 (180.8)	40 (12–70)
ITP before the treatment line		
Newly diagnosed	1	12.5
Persistent	1	12.5
Chronic	6	75.0
Concomitant diseases		
Autoimmune haemolytic anaemia	2	25.0
Antiphospholipid antibodies	1	12.5
Splenectomy	2	25.0
Thrombotic episodes	2	25.0
Spleen size (cm)	11 (2.6)	11.0 (8.5–13.0)
Bleeding score at ITP diagnosis		
1	2	25.0
2	2	25.0
3	4	50.0
Bleeding score before the treatment line		
0	2	25.0
1	0	0.0
2	5	62.5
3	1	12.5
Previous treatment lines	6.9 (1.8)	6.5 (5.5–8.0)
Steroids	8	100.0
IVIg	8	100.0
Azathioprine	8	100.0
Cyclosporine	7	87.5
MMF	4	50.0
Danazole	5	62.5
Splenectomy	2	25.0
TPO-RA		
Eltrombopag	5	62.5
Romiplostin	6	75.0
Awatrombopag	1	12.5
Study treatment line		
Rituximab + TPO-RA	8	100.0
Eltrombopag (50 or 75 mg)	2	25.0
Romiplostin (10 µg)	5	62.5
Awatrombopag (40 mg)	1	12.5

Table 4 Line characteristics in the study cohort by occurrence of CR (n = 8)

Analyzed trait	Statistical parameter	
	n M (SD)	% Me (Q ₁ –Q ₃)
PLT before treatment	28.9 (30.7)	16.5 (4.0–52.5)
IPF (%) before treatment	28.8 (25.3)	24.0 (18.0–30.0)
PLT after treatment	365.4 (634.7)	92.0 (39.5–392.5)
IPF (%) after treatment	14.0 (8.8)	14.0 (7.0–21.0)
PLT after 1 month	175.4 (183.0)	130.5 (15.0–306.0)
PLT after 6 months	181.7 (148.8)	117.0 (80.0–327.0)
PLT fastest response	509.1 (623.5)	243.0 (158.0–549.0)
PLT the highest value	670.7 (598.5)	447 (243–925)
Time to response (TTR) (day)	15.3 (11.6)	12.00 (3.0–26.0)
Time to best response (day)	15.3 (11.6)	12 (3–26)
Loss of response	1	14.3
Relapse-free survival (RFS)	5	71.4
RFS after 24 months	4	50.0
RFS time (month)	13.0 (8.4)	11.5 (6.0–20.0)
TFR in general	4	50.0
TFR after 1 month	7	87.5
TFR time (day)	115.5 (75.7)	138.0 (59.0–172.0)
Significant bleeding	0	0.0
Bleeding	3	37.5
Rescue medication	3	37.5
Urgent hospitalization	3	37.5
Side effects	1 ^a	12.5
Thrombotic episodes	0	0.0



REFRACTORY PATIENTS AND FOSTAMATINIB

Patients had received a median of **four prior therapies** (range 2–7). Twenty-nine **(91%)** patients had received a **prior TPO receptor agonist**, including 13 patients (41%) who had received at least two different TPO receptor agonists prior to fostamatinib.

Table 1 Baseline characteristics

	N = 31
Age (years), median (range)	50 (25–88)
Sex, n (%)	
Male	13 (42)
Female	18 (58)
Race/Ethnicity, n (%)	
White	22 (71)
Black	5 (16)
Hispanic	3 (10)
Unknown	1 (3)
Number of prior therapies, median (range)	4 (2–7)
Prior therapies, n (%)	
Corticosteroids	31 (100)
Intravenous immune globulin	23 (74)
Rituximab	22 (71)
Romiplostim	19 (61)
Eltrombopag	15 (48)
Avatrombopag	3 (10)
Splenectomy	6 (19)
Mycophenolate	3 (10)
Danazol	2 (6)
Ibrutinib	1 (3)
Baseline platelets, n (%)	
< 15 000/μl	10 (32)
15 000–30 000/μl	12 (39)
>30 000/μl	9 (29)

Table 2 Results

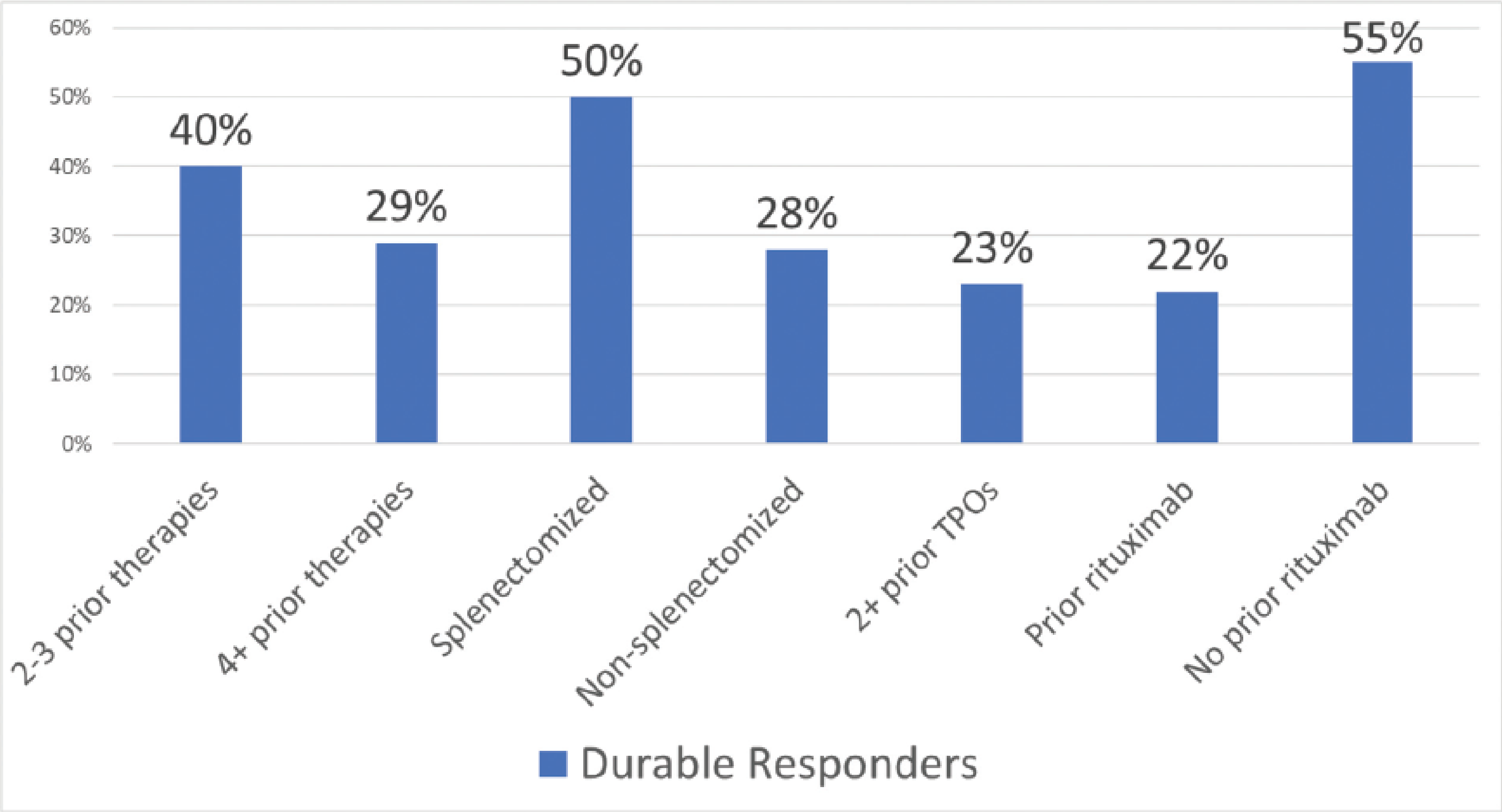
	N = 31
Response rates, n (%)	
Early response	11 (35)
Initial response	6 (19)
Durable response	10 (32)
Overall response	14 (45)
Time to response, median (range)	9 (4–55)
Dose adjustment, n (%)	24 (77)
Time to dose adjustment, median (range)	35 days (19–337)
Discontinuation reason, n (%)	
Refractory	19 (61)
Adverse event	4 (13)
Pregnancy	1 (3)
Normalized platelets	1 (3)

Thirteen patients (**42%**) received rescue therapy following initiation of fostamatinib.

Companion therapy was concomitantly administered to seven patients (**23%**) with fostamatinib.

The most common reason for discontinuation was having ITP **refractory to fostamatinib (n=19; 61%)**. Four patients (13%) discontinued therapy due to an adverse event (n=2, diarrhea; n=1, hypertension, n=1, transaminitis). The most common adverse events were hypertension (n=4; 13%) and diarrhea (n=4; 13%).

Fig. 1



Subgroups that achieved a **higher rate of durable responses** included those who had received **two to three prior therapies** (n=4/10; 40%), splenectomized patients (50%), and those who had **not received prior rituximab** (n=5/9; 55%).

AVATROMBOPAG + FOSTAMATINIB

Eighteen patients received treatment with AVA and FOS in combination between August 2022 and January 2024. **Refractoriness** was defined as a lack of any or durable response despite the use of maximum recommended doses of a drug.

During the study period, a total of 112 patients received treatment with AVA in Spanish centres and Norwegian ITP registry. In 28 of 112 patients (25%), there was no response after 2 or more weeks with AVA 280 mg weekly. In 18 of these 28 patients, FOS was combined with AVA.

TABLE 1 Characteristics of patients and description of the response.

Patient identification	Sex	Age at combination (years)	Time from ITP diagnose to combination (months)	Type ITP	Number previous treatment lines	Previous AntiCD20	Previous ELT	Previous ROM	Platelet at start combination (×10e9/L)
1	Male	40	7	Persistent	5		Yes	Yes	26
2	Male	60	38	Chronic	8	Yes	Yes	Yes	21
3	Male	69	48	Chronic	8	Yes	Yes	Yes	14
4	Male	34	12	Chronic	7	Yes	Yes	Yes	12
5	Male	69	50	Chronic	4		No	Yes	11
6	Male	63	59	Chronic	7	Yes	Yes	Yes	13
7	Male	50	10	Persistent	6		Yes	Yes	18
8	Female	76	19	Chronic	4		Yes	Yes	5
9	Male	60	2.3	Newly diagnose	3		No	No	21
10	Female	16	17	Chronic	3		Yes	Yes	25
11	Male	59	28	Chronic	5		Yes	Yes	8
12	Male	85	10	Persistent	4		No	No	10
13	Female	74	72	Chronic	7		Yes	Yes	13
14	Female	30	56	Chronic	4		Yes	Yes	10
15	Male	61	8	Persistent	4		No	Yes	21
16	Male	28	4	Persistent	4		No	Yes	9
17	Male	86	15	Chronic	4		Yes	No	15
18	Male	28	28	Chronic	5		No	Yes	18

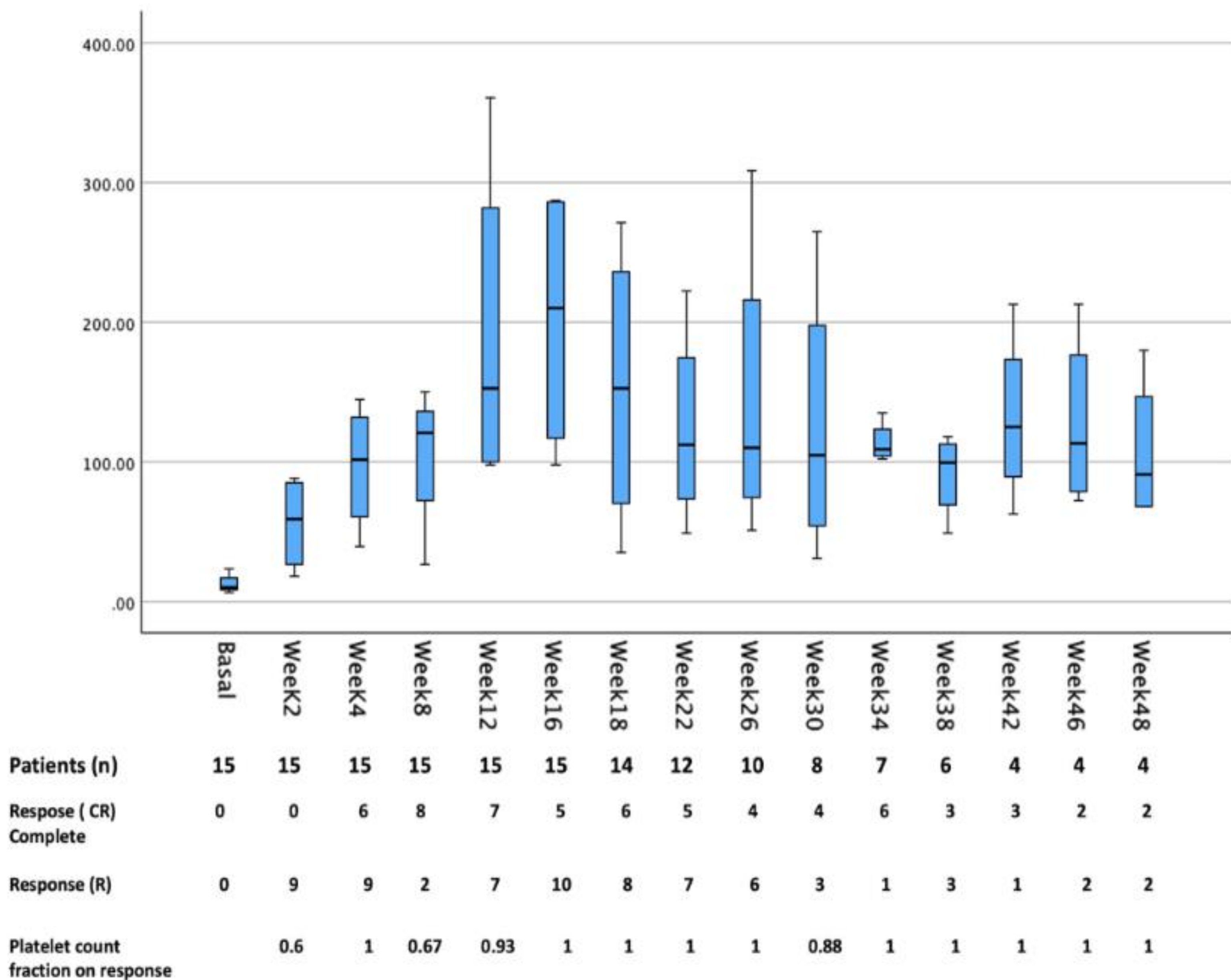
Abbreviations: AVA, avatrombopag; CR, complete response; ELT, eltrombopag; FOS, fostamatatinib; ITP, immune thrombocytopenia; n.a., no applicant; NR, no response; R, response; ROM, romiplostim.

The overall response was achieved in 15 out of 18 patients (83.3%) with 8 achieving a CR.

The median time from combination start to R of 15 days (IQR: 12–69 days) and CR of 15 days (IQR:8–35 days).

In patients who achieved R, the median dose at that point was AVA 280 mg per week and FOS 2100 mg per week. In those who achieved CR, the median dose of AVA was 280 mg per week and FOS of 1400 mg per week.

In 4 of 5 patients who lack response, relapse occurred during tapering of AVA (4 patients) and/or FOS (3 patients). After re-introducing previous doses of AVA and/or FOS, 4 patients achieved a response again.



Adverse events were observed in 6 of the 18 patients (33%).

AVA related: *headache* and a WHO grade 2 *liver toxicity* which was resolved after the interruption of AVA for 6 days and reintroduction at a lower dose, from 140 to 60 mg weekly.

FOS related: *diarrhoea* grade I was reported in three patients, and these were resolved without reduction or stopping the drug only with initial diet restrictions.

Two patients presented grade IV *neutropenia* considered to be related to FOS by investigators. Neutropenia was recovered after 2 weeks of FOS was stopped. FOS was re-started in both patients, but neutropenia grade III appeared in one of them ,FOS was stopped in this case, and the patient lost response.

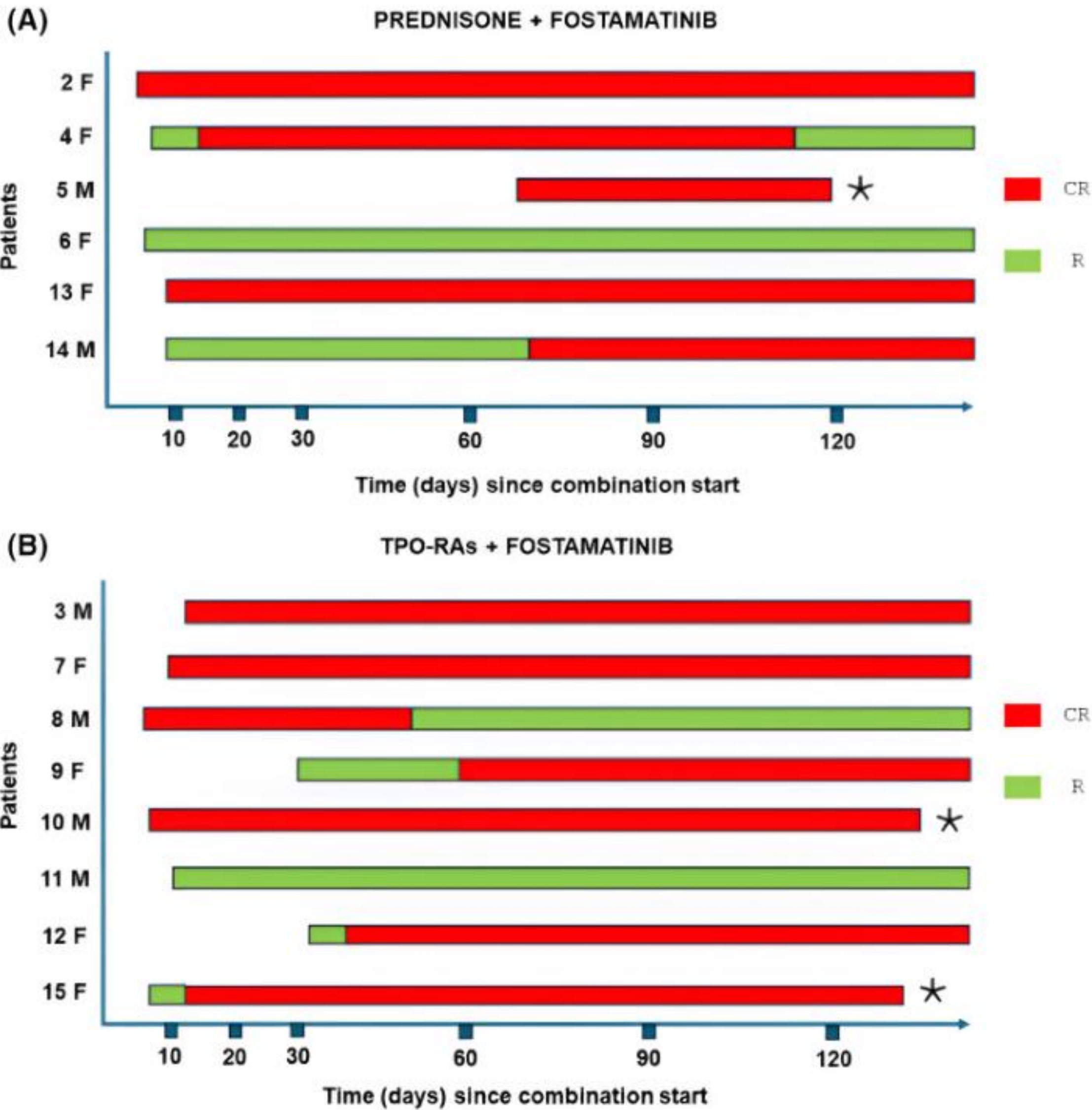
Tossicità accettabile

TABLE 1 Patients characteristics.

Patients characteristics	
Females, <i>n</i> (%)	9 (60)
Age, median (IQR)	55 (50–63)
Lines of therapy, median (range)	4 (2–7)
Combination therapy	
Prednisone, <i>n</i> (%)	7 (47)
Eltrombopag, <i>n</i> (%)	2 (13)
Romiplostim, <i>n</i> (%)	6 (40)
Platelets pre fostamatinib ($\times 10^9/L$), median (IQR)	23 (6–26)
Response, <i>n</i> (%)	12 (80)
Complete response, <i>n</i> (%)	11 (73)
Time to response (days), median (IQR)	9 (7–19)
Time to best response (days), median (IQR)	13 (8–40)
Combined treatment duration, median (IQR)	119 (38–245)
Combined treatment discontinuation ^a , <i>n</i> (%)	6 (40)
Response at the last follow-up, <i>n</i> (%)	12 (80)

Abbreviations: IQR, interquartile range; *n*, number.

^aFor sustained response.





C.C.
63 y.o
No significant
medical history

2016

PLTs 20,000/mm³

Corticosteroids at varying
doses, with a maximum platelet
count of 50,000/mm³.



Jan 2023

PLTs 25,000/mm³

Prednisone 15 mg per day was
added, with a maximum platelet
count of 41,000/mm³.
The patient experienced an
episode of cholecystitis for which
cholecystectomy was required.



Oct 2022

PLTs 15,000 /mm³

Eltrombopag was started and
progressively increased up to 75
mg/day, with a maximum
platelet count of 45,000/mm³



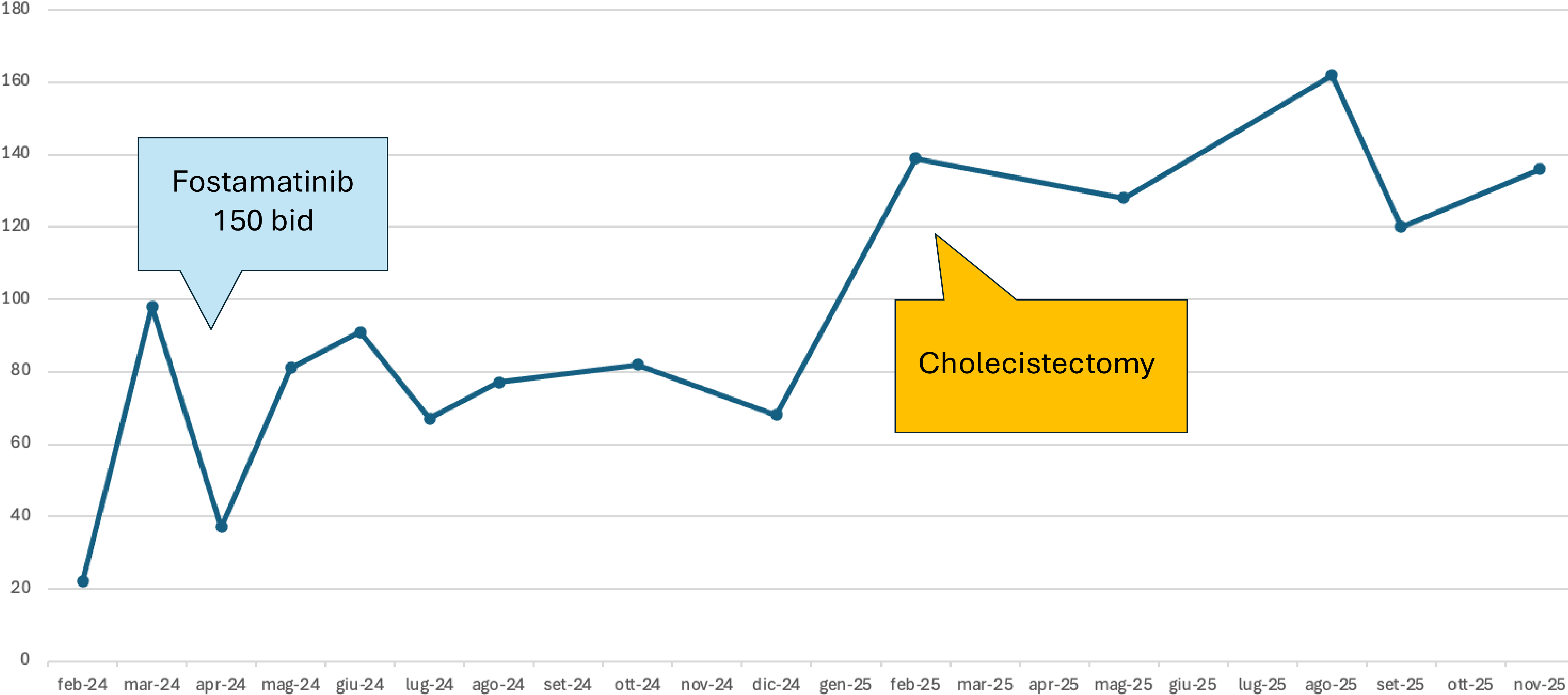
Feb 2024

PLTs 22,000/mm³

Start Fostamatinib 100 mg/bid



Platelet count



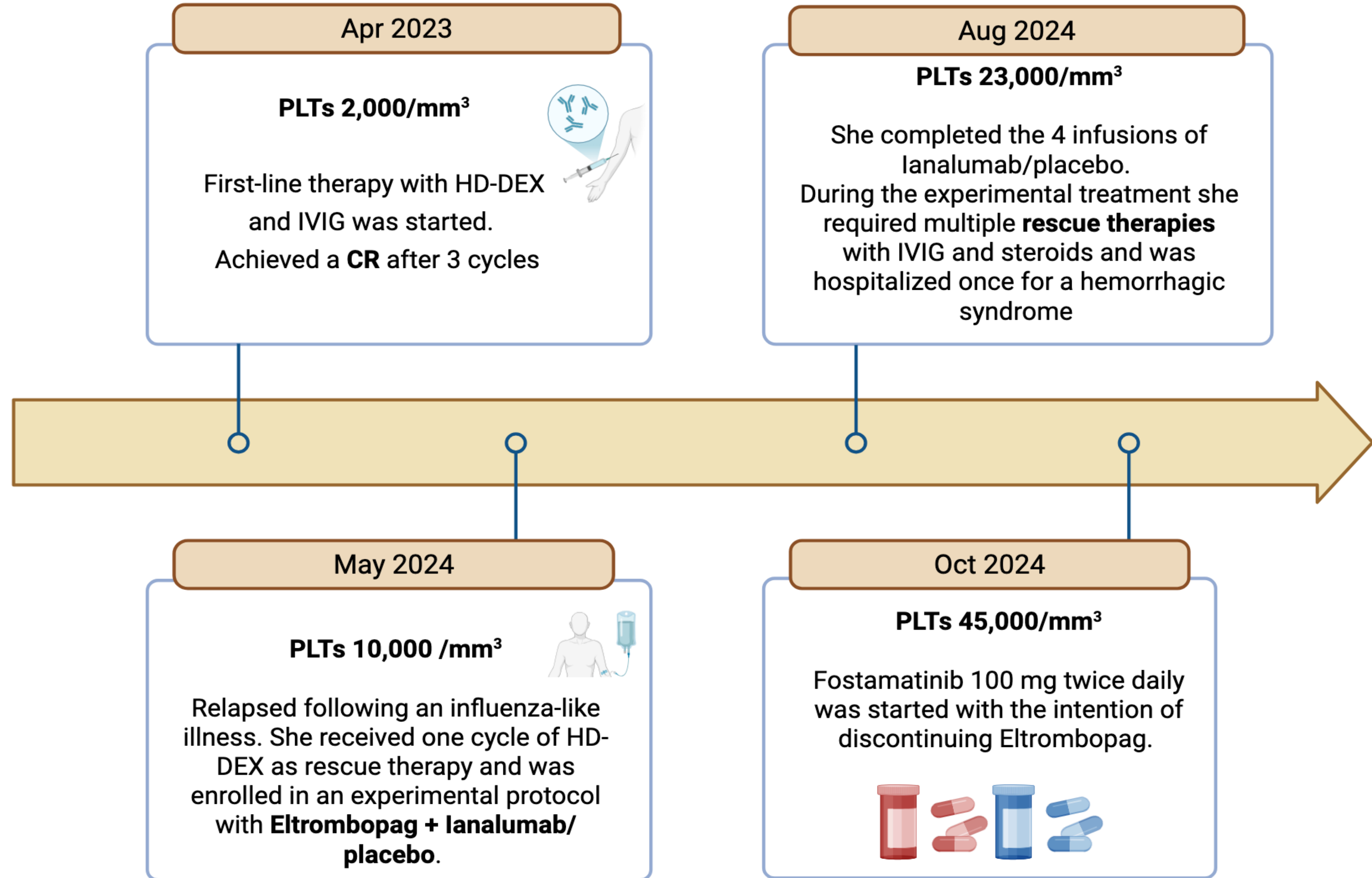
Comments

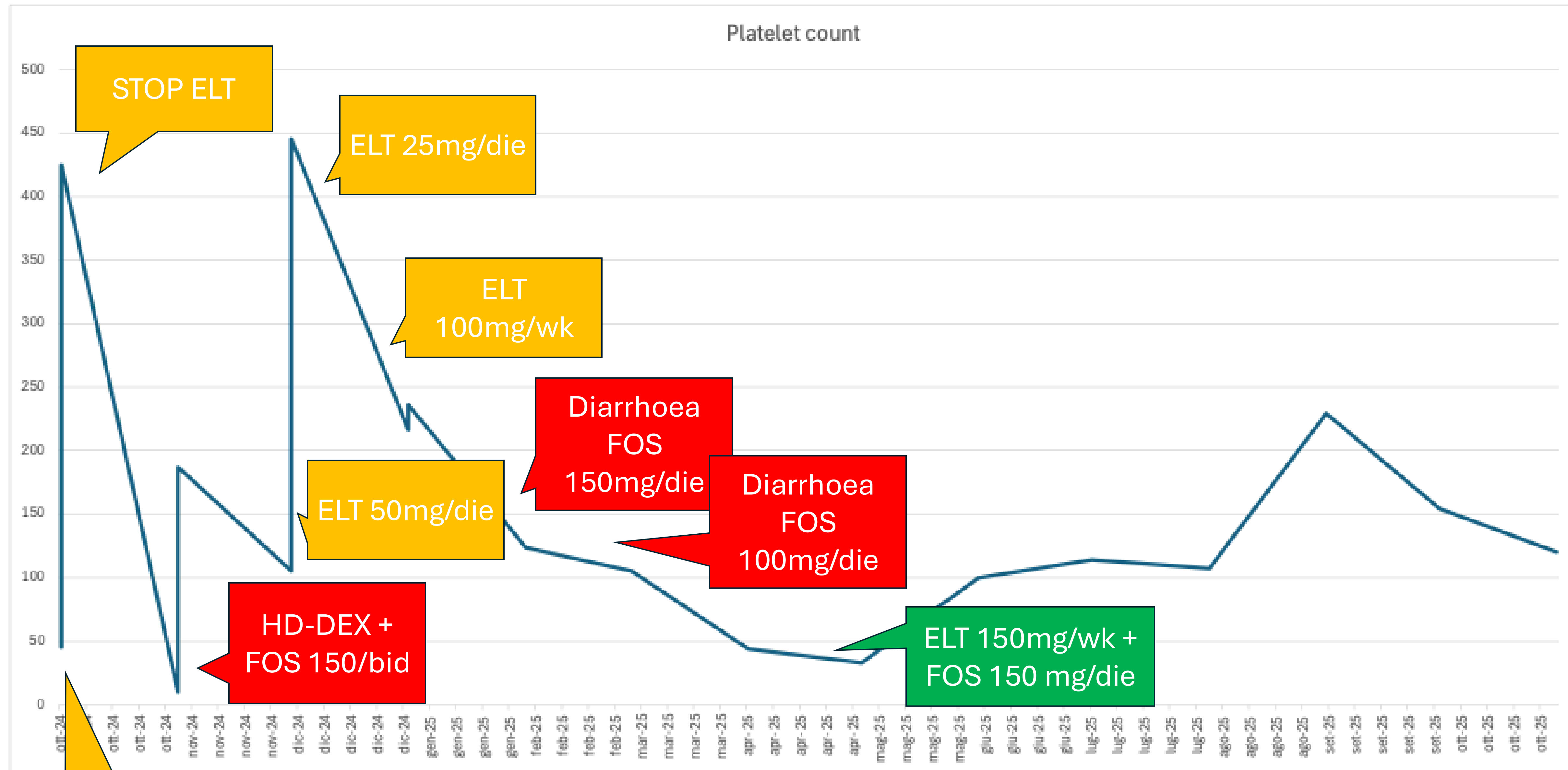
- Paziente definibile refrattaria?
- Perché non altro TPO prima di Fostamatinib?



S.E.
65 y.o
Arterial hypertension,
hypercholesterolemia,
glaucoma.

She works as a kindergart
teacher.





ELT 75mg/die

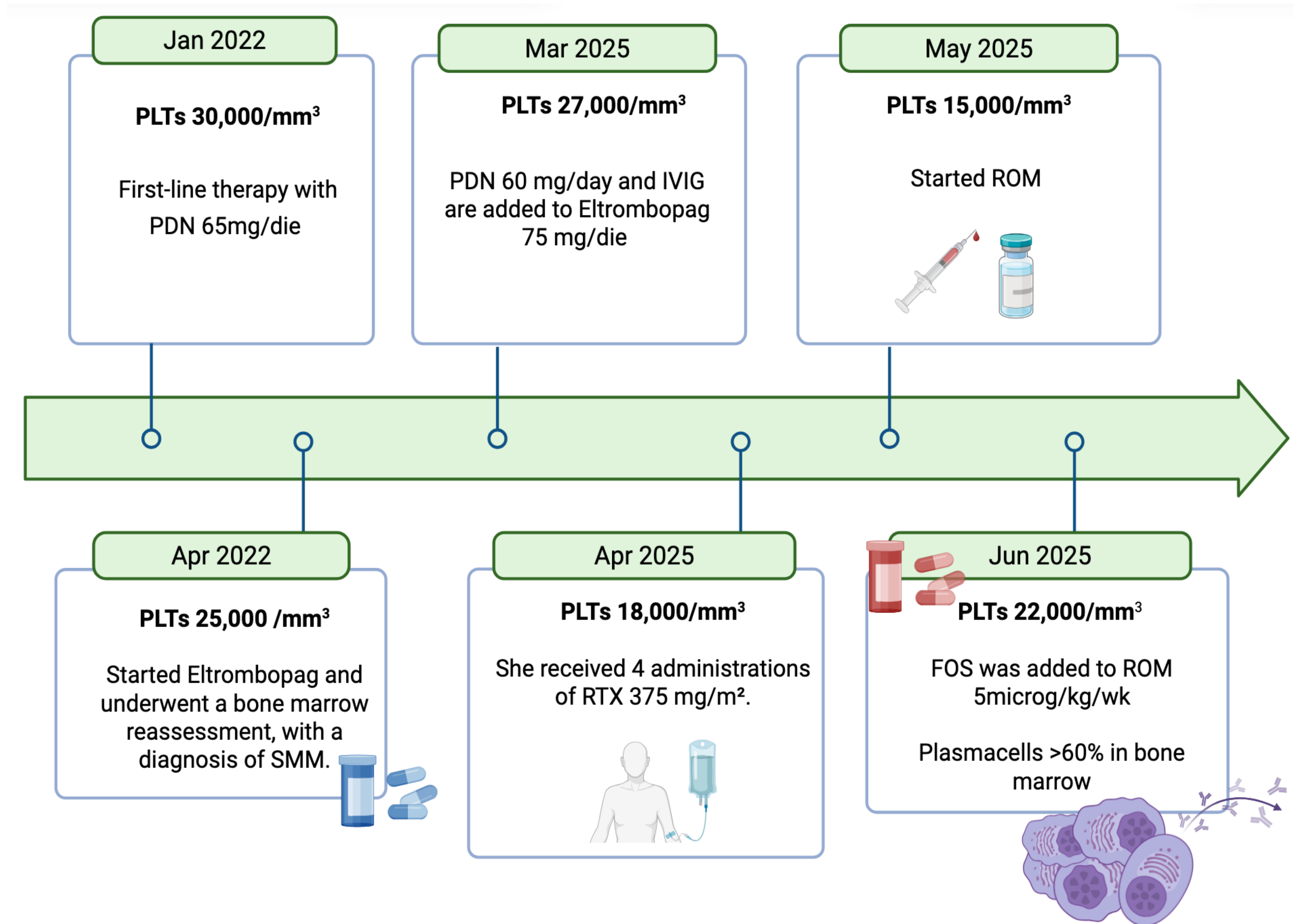
Comments

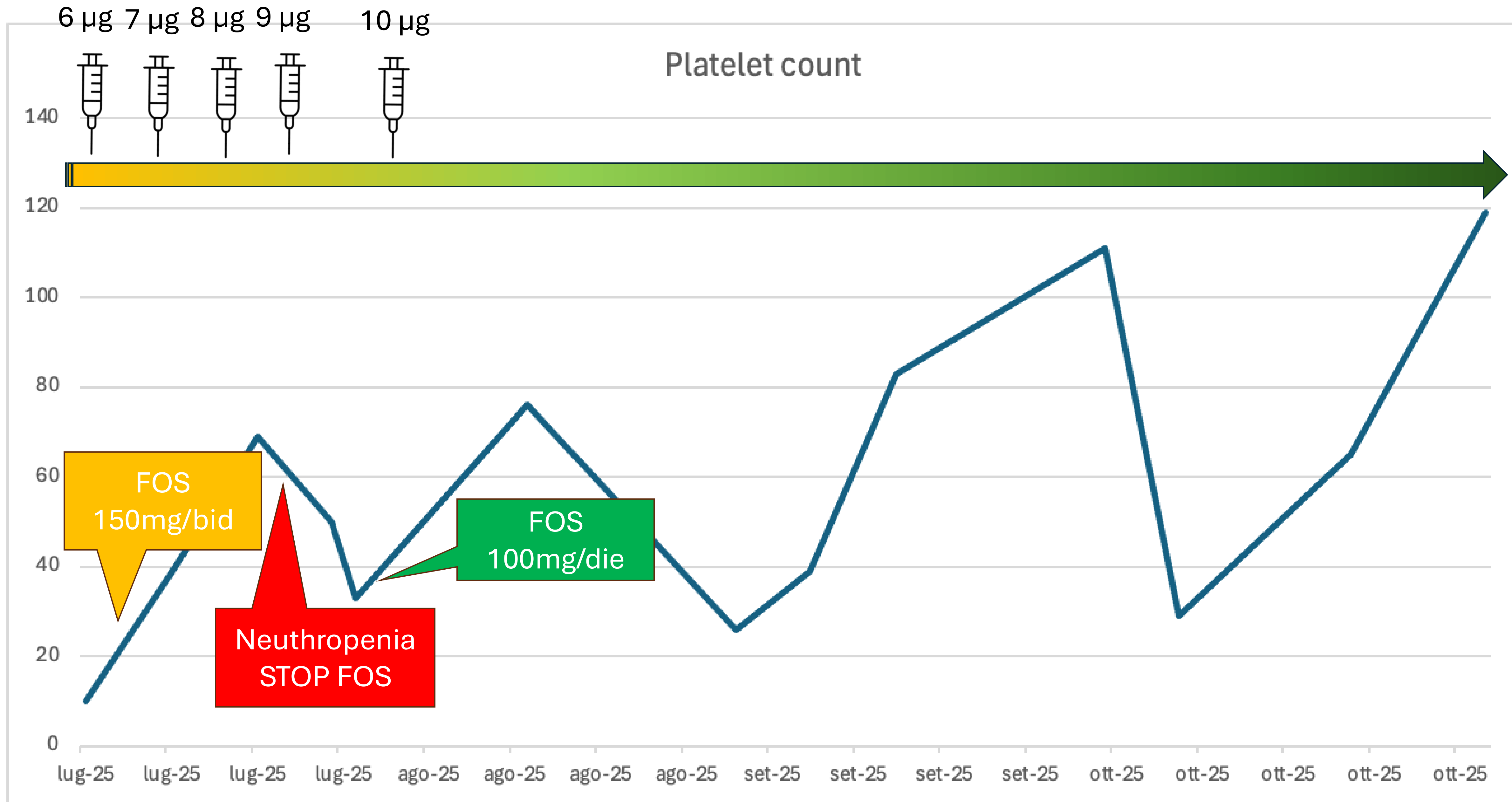
- Non riuscita sospensione TPO
- Minori dosi di TPO → minori oscillazioni piastriniche
- Minori dosi di FOSTA → minori effetti collaterali
- Combinazione → ridotti episodi di ospedalizzazione



G.N.
68 y.o
Medical history includes
fibromyalgia and restless
legs syndrome.

She has been in follow-up
for **MGUS IgGk** since
2009.





Comments

- ITP in discrasia plasmacellulare
- Neutropenia limitante sul dosaggio Fostamatinib
- Non più ospedalizzazioni (fino alla combo numerosi ricoveri)
- Rituximab # Fostamatinib