Real world data with Fostamatinib in ITP patients

María Eva Mingot Castellano, MD PhD

Hematology Department, University Hospital Virgen del Rocío, Instituto de Biomedicina de Sevilla, Universidad de Sevilla, Spain.

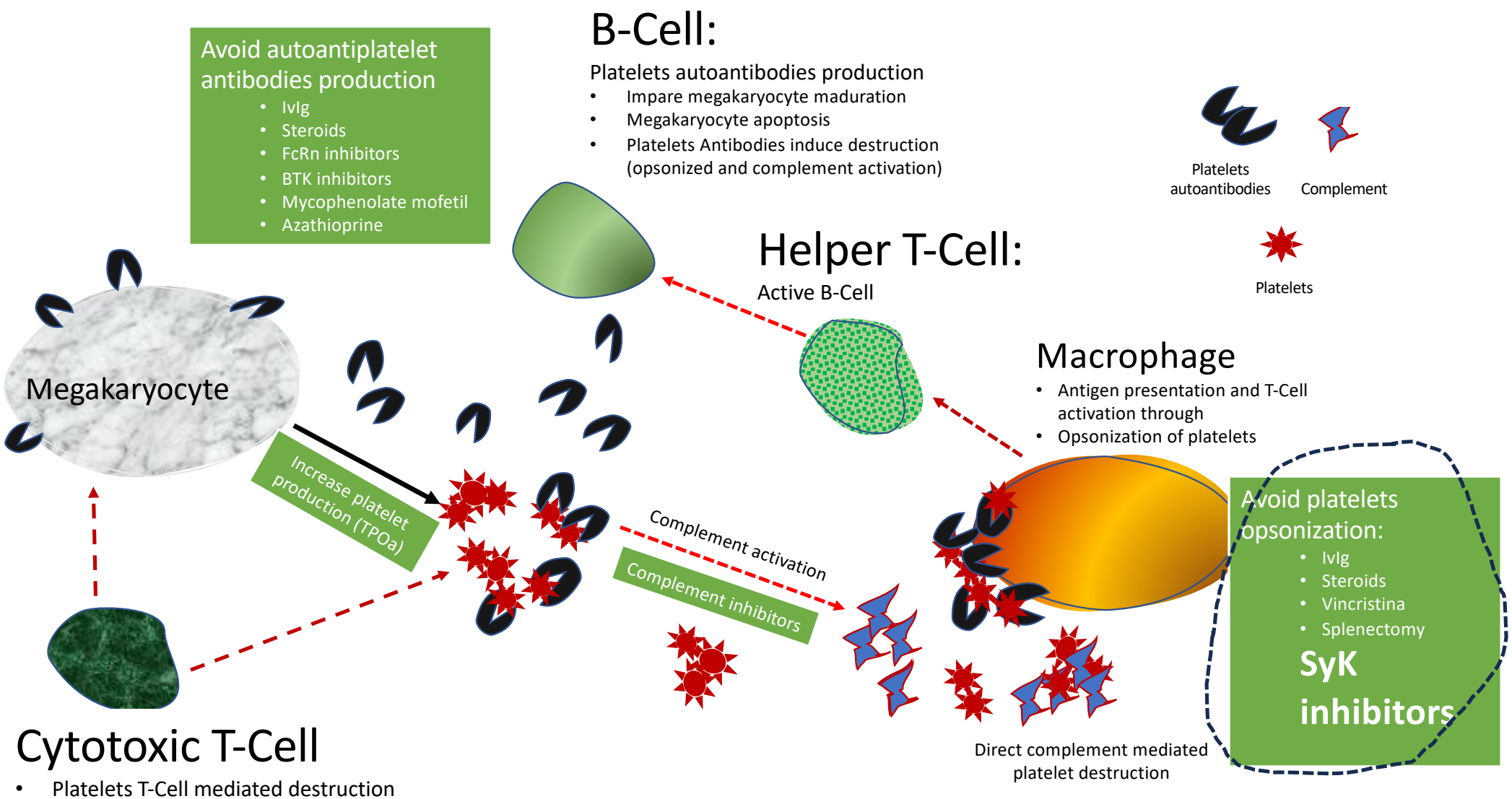
Medical Director of Diagnostic Area, Univeristy Hospital Virgen del Rocío, Sevilla, Spain

Disclosures of María Eva Mingot Castellano

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Amgen	X		X		X	X	
Argenix			X			X	
Boehringer			X			X	
Grifols	X		X		X	X	
Novartis	X		X		X	X	
Novo Nordisk	X		X		X	X	
Sanofi	X		X		X	X	
Shiomi			X				
Sobi	X		X		X	X	
Takeda	X		X		X	X	

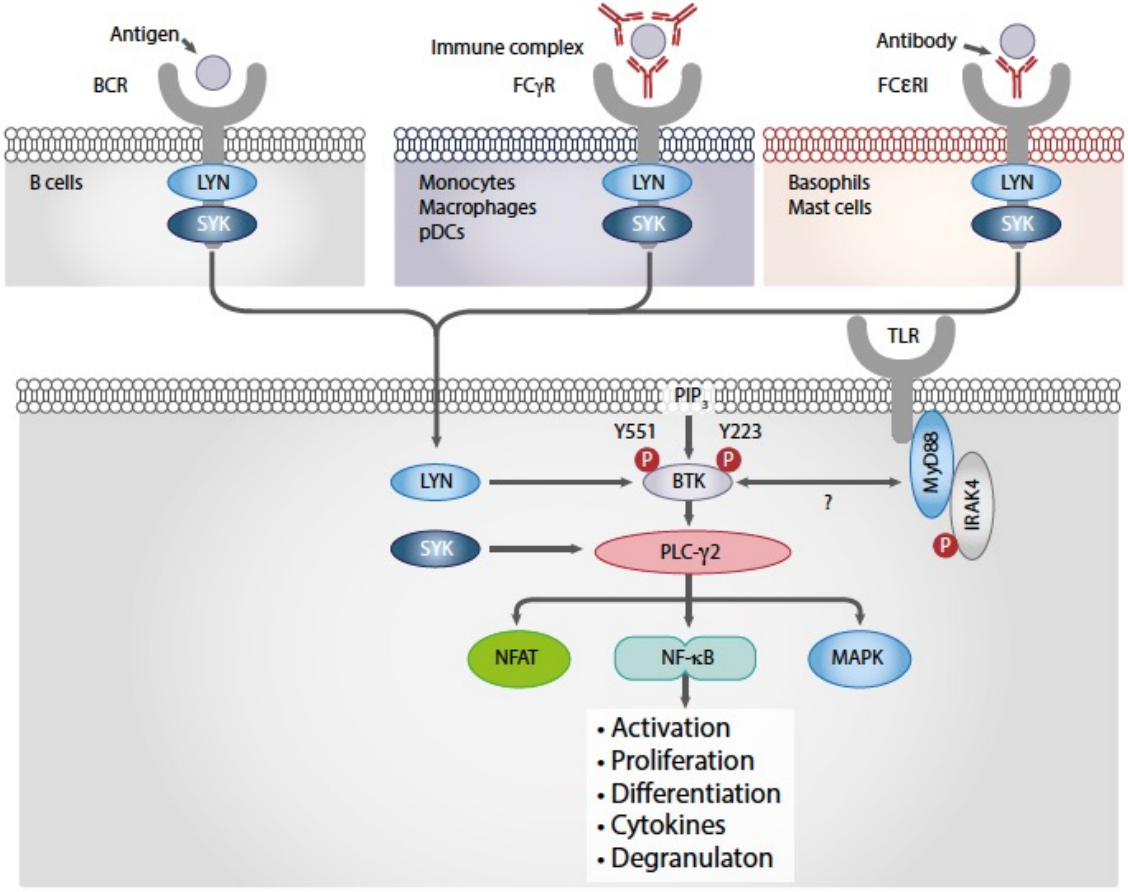
Committees:

Member of Scientific Committee of SETH (Sociedad Española de Trombosis y Hemostasia), Member of Director Committee of Fundación Victoria Eugenia, Member of Director Committee of CAT, Member of Director Committee of GEPTI, Member of Director Committee of REPTT-GEA



Mingot-Castellano ME, et al. Pharmaceuticals (Basel). 2022 Jun 23;15(7):779.

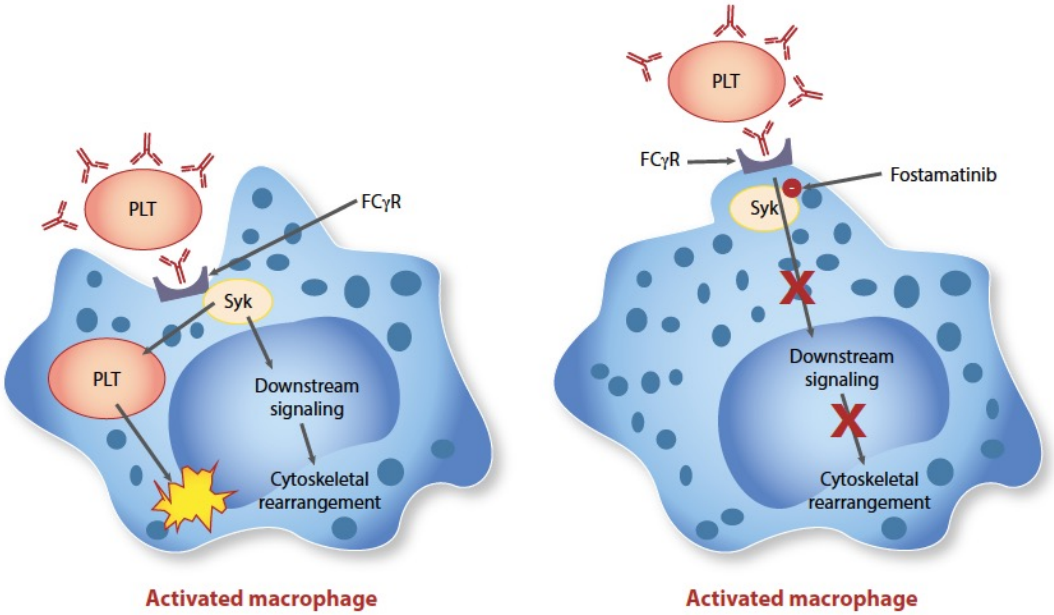
What is Spleen Tyrosine Kinase (SYK)?



- Spleen tyrosine kinase (SYK).
- Cromosome 9q22, 635 aa, 72 kDa.
- FcγRs active SYK
- SYK active a signs cascade
- Change in cytoskeleton and phagocytosis
- SYK Induces:
  - Lymphocite B activation
  - Antibodies production
  - Activation fo GPVI y CLEC-2 (platelet activity)

Zarrin AA, et al. Nat Rev Drug Discov. 2021 Jan;20(1):39-63
Liu D, et al. J Hematol Oncol. 2017 Jul 28;10(1):145

What is Fostamatinib? Tyrosine Kinase inhibitor



- Active metabolite of Fostamatinib: R406
- Able to block platelet destruction induced by antibodies (similar to immunoglobulins)

Newland A, et al. Immunotherapy. 2020 Dec;12(18):1325-401
Liu D, et al. J Hematol Oncol. 2017 Jul 28;10(1):145
Podolanczuk A, et al. Blood 2009; 113: 3154–3160.

FOSTAMATINIB: STUDIES FIT-1/FIT-2

FIT-1/FIT-2: Randomized control/placebo, doble blinded

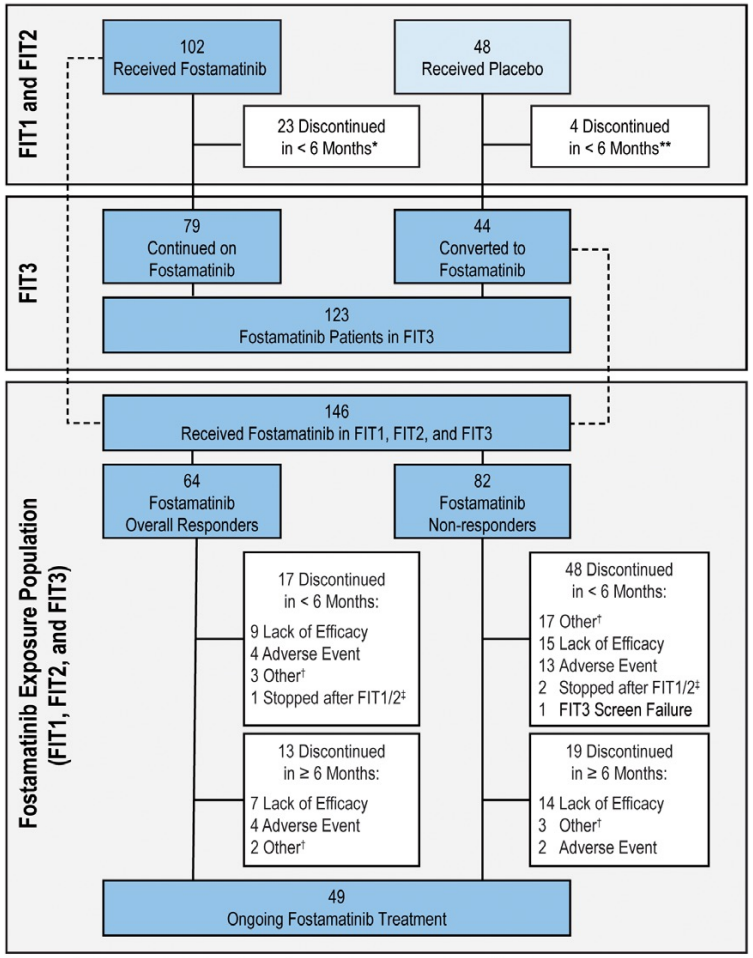
- Median time to response: 15 days[1]

Global response: 43%[1,2,†]

- Almost one week count ≥50.000/µl during weeks 0-12

Stable response: 17%[1,3]

- ≥50.000/µl during weeks 14-24 (4 to 6 consecutives visits)
- Median platelet counts at week 24 in responders: 95.000/µl

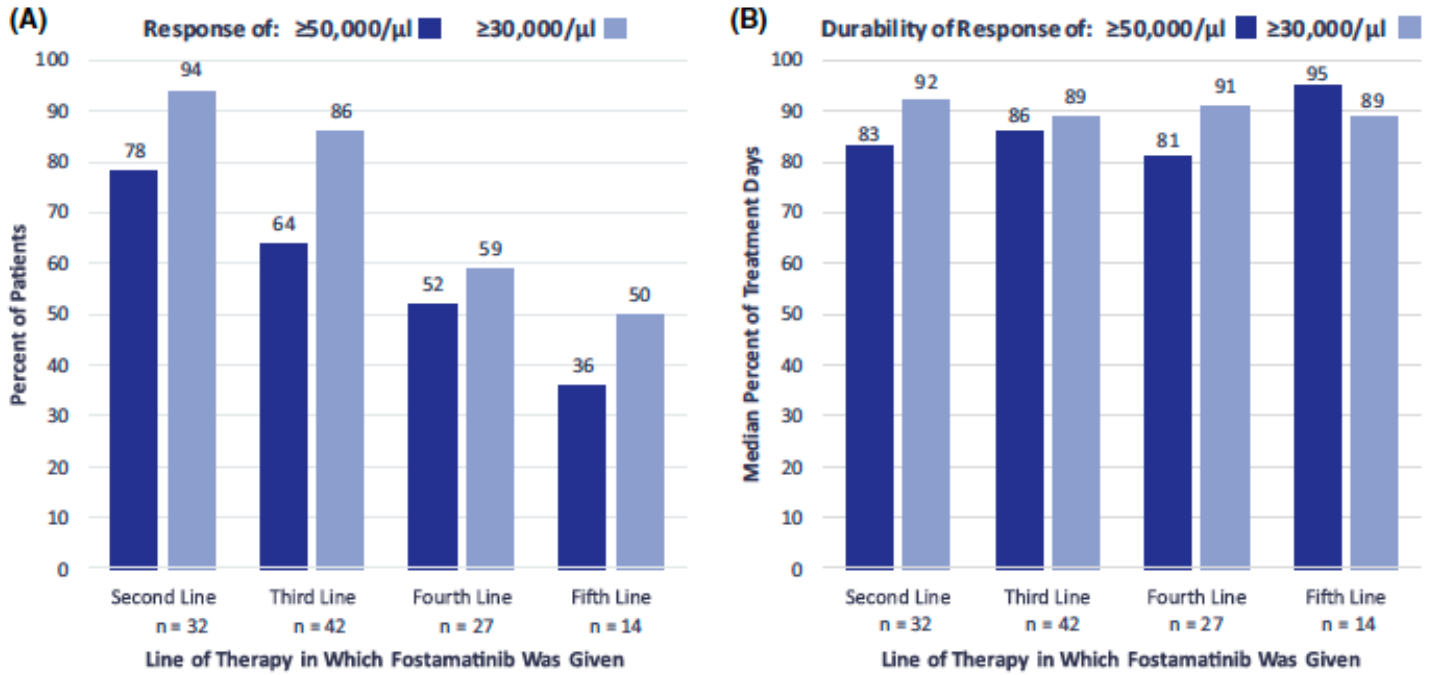


* Reasons for discontinuation included in total fostamatinib exposure population information
** 4 discontinued due to AEs
† Other may include: lost to follow-up, non-compliance, physician decision, subject decision
‡ After completing initial study (FIT1 or FIT2), patient chose not to enter extension study

1. Bussel J, et al. *Am J Hematol*. 2018;93(7):921-30.
2. Cooper N, et al. *Ther Adv Hematol.* 2021;12:1-12 3. Bussel JB, et al. *Am J Hematol*. 2019;94(5):546-53.

What to wait from Fostamatinib

- The sooner the better
- Patients who response maintained this response, high stability



Boccia R, et al. Br J Haematol. 2020 Sep;190(6):933-938.

Fostamatinib in PTI: Safety profile

Diarrhoea 31%, HTA 28%, Nausea 19%, neutropenia 6%

Adverse reaction	Fostamatinib (*N* = 102)				Placebo (*N* = 48)			
	Mild %	Moderate %	Severe %	Total %	Mild %	Moderate %	Severe %	Total %
Any AE	32	35	16	83	42	19	15	75
Diarrhea[a]	21	10	1	31	13	2	0	15
Hypertension[b]	17	9	2	28	10	0	2	13
Nausea	16	3	0	19	8	0	0	8
Dizziness	8	2	1	11	6	2	0	8
ALT increased	5	6	0	11	0	0	0	0
AST increased	5	4	0	9	0	0	0	0
Respiratory infection[c]	7	4	0	11	6	0	0	6
Rash[d]	8	1	0	9	2	0	0	2
Abdominal pain[e]	5	1	0	6	2	0	0	2
Fatigue	4	2	0	6	0	2	0	2
Chest pain	2	3	1	6	2	0	0	2
Neutropenia[f]	3	2	1	6	0	0	0	0

[a]Includes diarrhea and frequent bowel movement.
[b]Includes hypertension, blood pressure (BP) increased, BP diastolic abnormal, and BP diastolic increased.
[c]Includes upper respiratory tract infection, respiratory tract infection, lower respiratory tract infection, and viral upper respiratory tract infection.
[d]Includes rash, rash erythematous and rash macular.
[e]Includes abdominal pain, and abdominal pain upper.
[f]Includes neutropenia and neutrophil count decreased.
ALT, alanine aminotransferase; AST, aspartate aminotransferase.
Note: Common adverse reactions defined as all adverse reactions occurring at a rate of ≥ 5% of patients in the fostamatinib group and greater than placebo rate.

Bussel J, et al. Am J Hematol. 2018 Jul;93(7):921-306
Kuwana M, et al. Am J Hematol. 2024 Feb;99(2):E55-E59.

Fostamatinib in ITP: Safety profile

- After 5 years follow up, 146 patients with PTI, 229 patients/year
- 0,7% vascular events*
- Median 2 cardiovascular risk factors (0-7)
- 87% 1 cardiovascular risk factor
- 58% 2 or more cardiovascular risk factors

Eltrombopag*	Romiplostin*	Avatrombopag*
0-2,3%	2,4-8,9%	2,6-9,4%
Vascular events	Vascular events	Vascular events

* There is no head to head study, not feasible to compare

Cooper N et al. Ther Adv Hematol. 2021 Apr 30;12:20406207211010875.

Syk inhibitor fostamatinib: Real world experience

Transitioning From Thrombopoietin Agonists to the Novel SYK Inhibitor Fostamatinib: A Multicenter, Real-World Case Series

David M. Hughes, Charina Toste, Christopher Nelson, Juliet Escalon, Frances Blevins, Bhavesh Shah

J Adv Pract Oncol. 2021;12(5):508-517.

- There is no evidence from clinical trials regarding the alternation of second-line agents that do not require discontinuation in the previous weeks, nor the safety of combining fostamatinib with other second-line agents.
- In this case series, strategies for transitioning from TPO-RA to fostamatinib are provided, with some degree of overlap between both agents.

Real-World Use of Fostamatinib in Patients with Immune Thrombocytopenia and Thrombotic Risk

Amit R. Mehta, Aron Kefela, Charina Toste, Donald Sweet

Acta Haematol. 2022;145:221-228.

- In this study, a series of cases of patients with ITP and cardiovascular and thromboembolic risk factors is presented.
- The presentation and course of treatment for ITP were unique in each case. Despite this heterogeneity, all patients were successfully treated with fostamatinib without further thromboembolic events

The Efficacy and Safety of Fostamatinib in Elderly Patients with Immune Thrombocytopenia: A Single-Center, Real-World Case Series

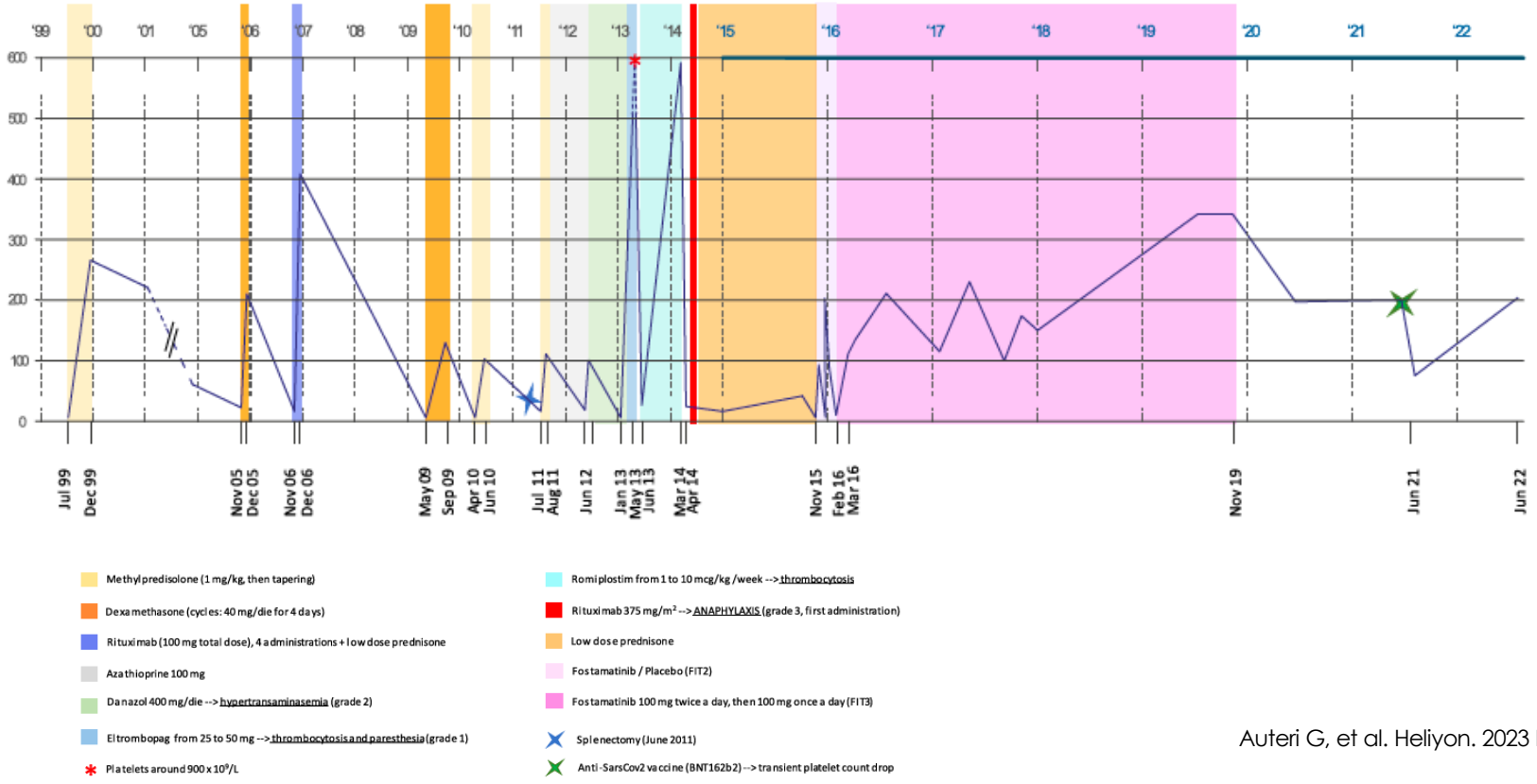
Jessica Liu, Cyrus C. Hsia

Adv Hematol. 2022 Nov 3;2022:8119270.

- This is the largest case series investigating the use of fostamatinib in an elderly population with ITP.
- In this retrospective review of patients aged ≥65 years, fostamatinib was effective and safe in the majority of patients

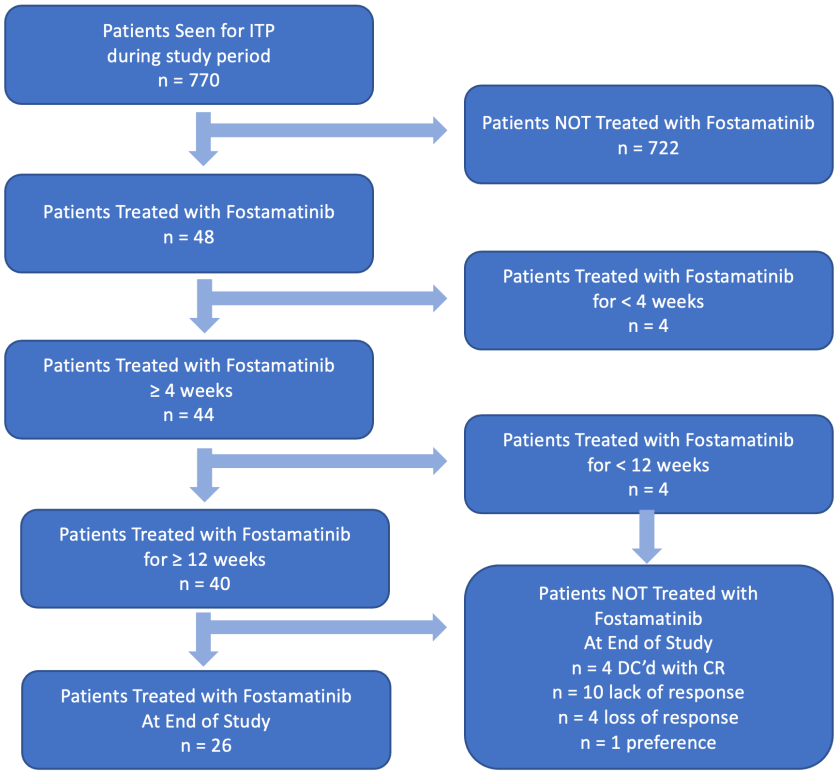
Syk inhibitor fostamatinib: Real world experience

Tapering and sustained response first experience



Auteri G, et al. Heliyon. 2023 Feb 4;9(2):e13462.

Real-World Use of Fostamatinib in Andalusia, Spain



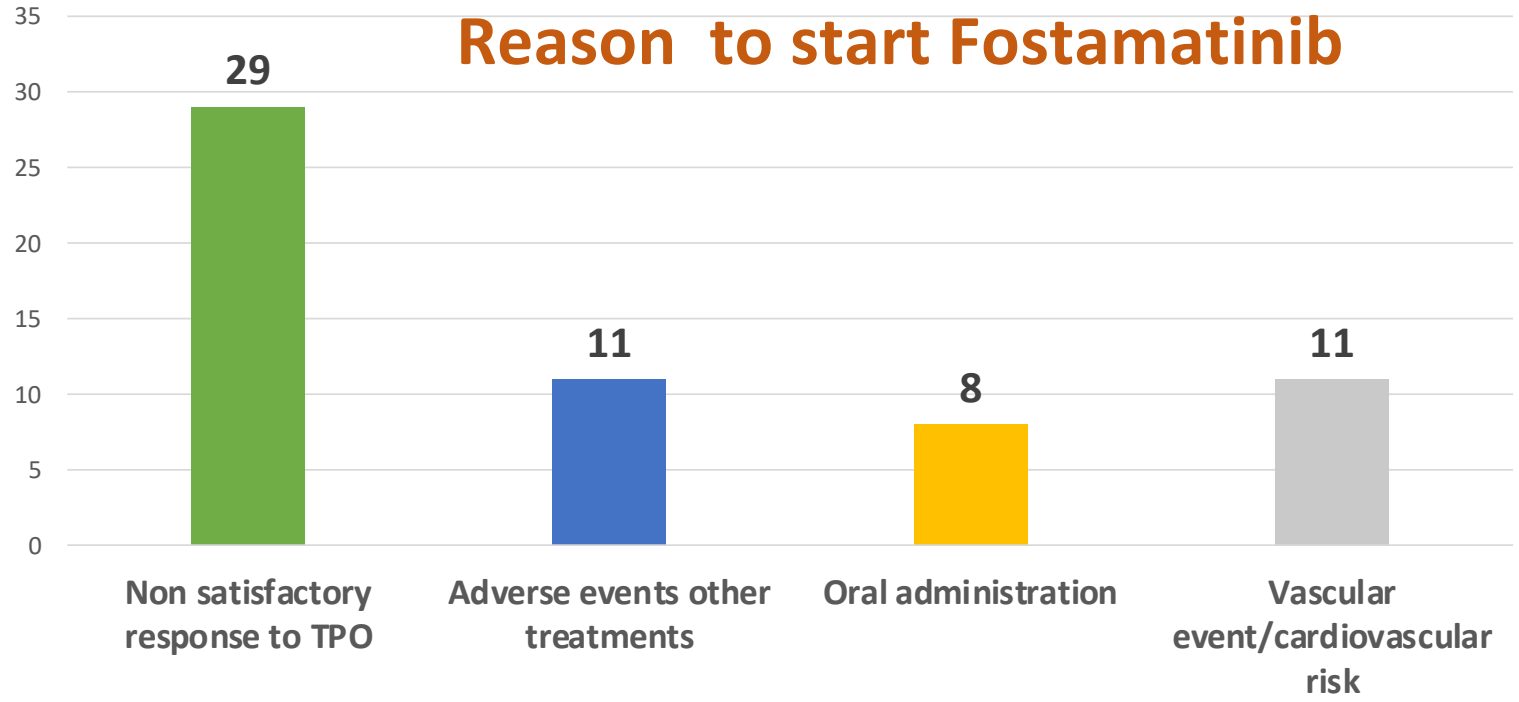
Characteristic/Demographic	n (%)
Total number of patients	44 (100)
Female	21 (47.7)
WHO Hemorrhagic Classification	
0 points	11 (25.0)
1 point	28 (63.6)
2 points	4 (9.1)
3 points	1 (2.3)
Age (yr)	58 (18-86)
Platelet count at diagnosis	11 × 10^9/L ((1-76 × 10^9/L)
Platelet count at baseline	15 × 10^9/L ((2-195 × 10^9/L)
Number of prior lines of treatments	4 (1-8)

Jiménez-Bárcenas R, et al. Br J Haematol. Br J Haematol. 2024 May;204(5):1977-1985.

Real-World Use of Fostamatinib in Andalusia, Spain

Type ITP:

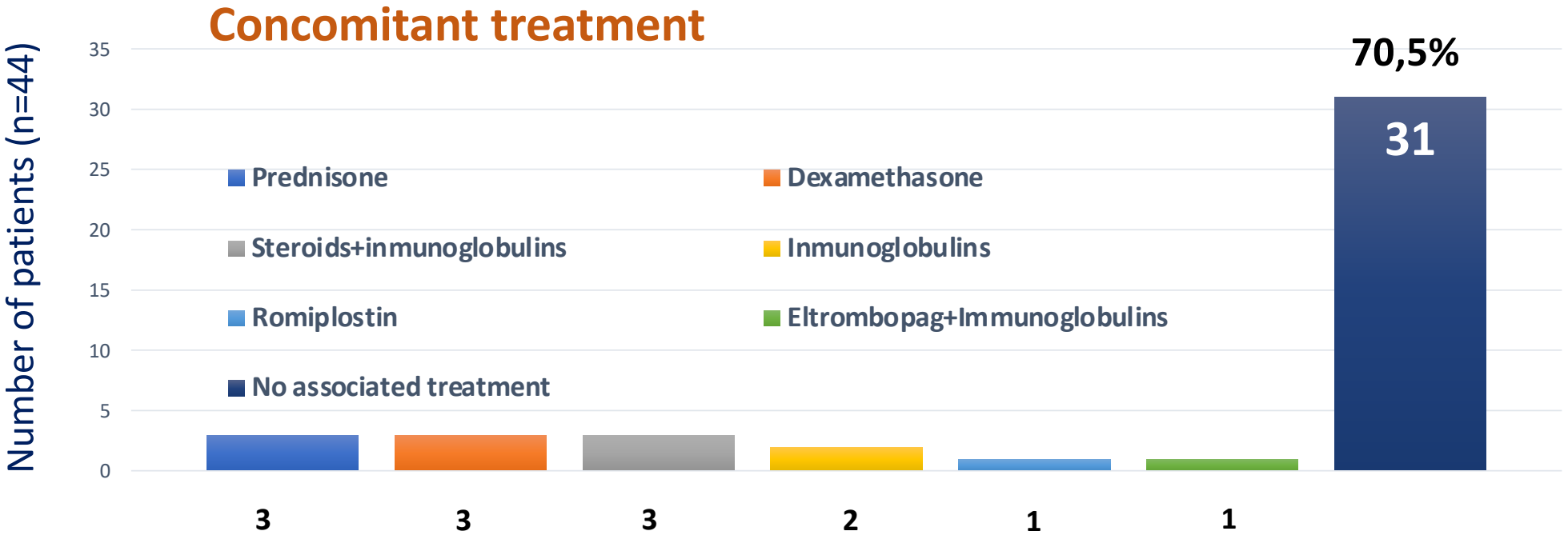
- Chronic: 35/44 (79.6%)
- Persistent: 6/44 (13.6%)
- Newly diagnosed: 3/44 (6.8%)



Jiménez-Bárcenas R, et al. Br J Haematol. Br J Haematol. 2024 May;204(5):1977-1985.

Real-World Use of Fostamatinib in Andalusia, Spain

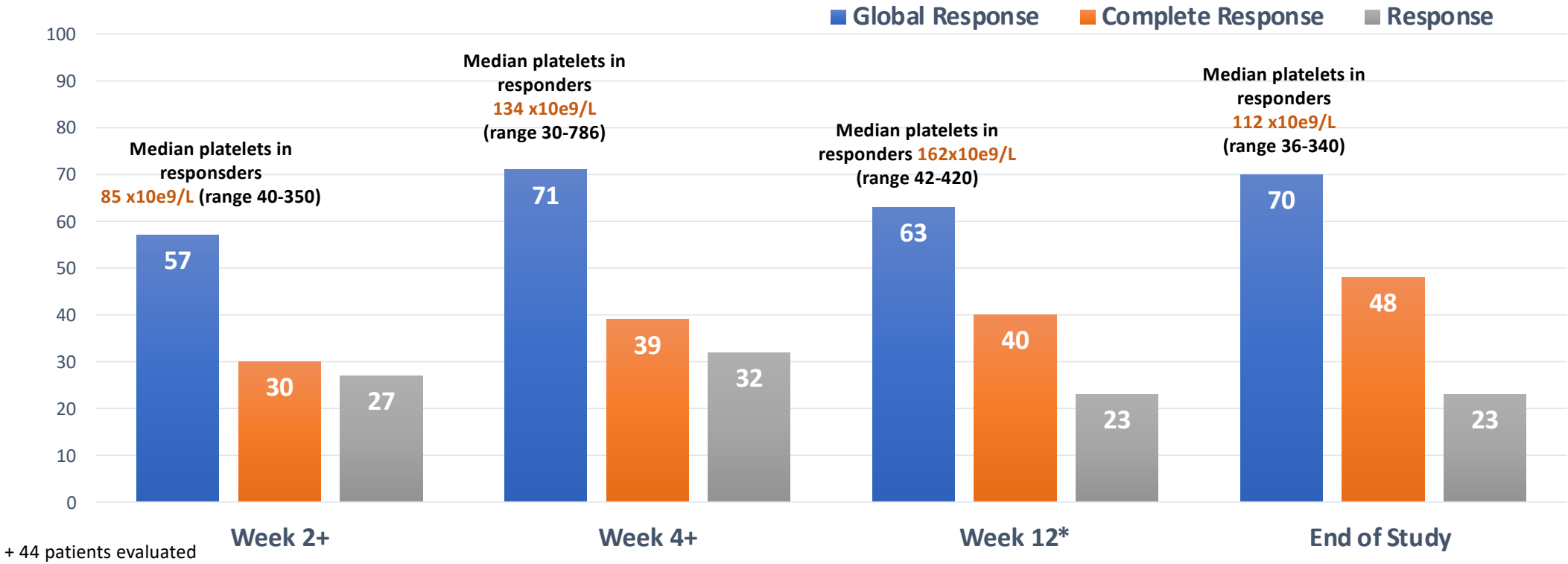
- Median platelet count baseline: 15 x10^9/L (range 2-195).
- Starting dose: 100 mg/12h (n=38); 150mg/12h (n=6).
- Increase of dose in 59% of patients, median time to increase 28 days (range 8-90 days).



Jiménez-Bárcenas R, et al. Br J Haematol. Br J Haematol. 2024 May;204(5):1977-1985.

Real-World Use of Fostamatinib in Andalusia, Spain

Evolution of response (%)

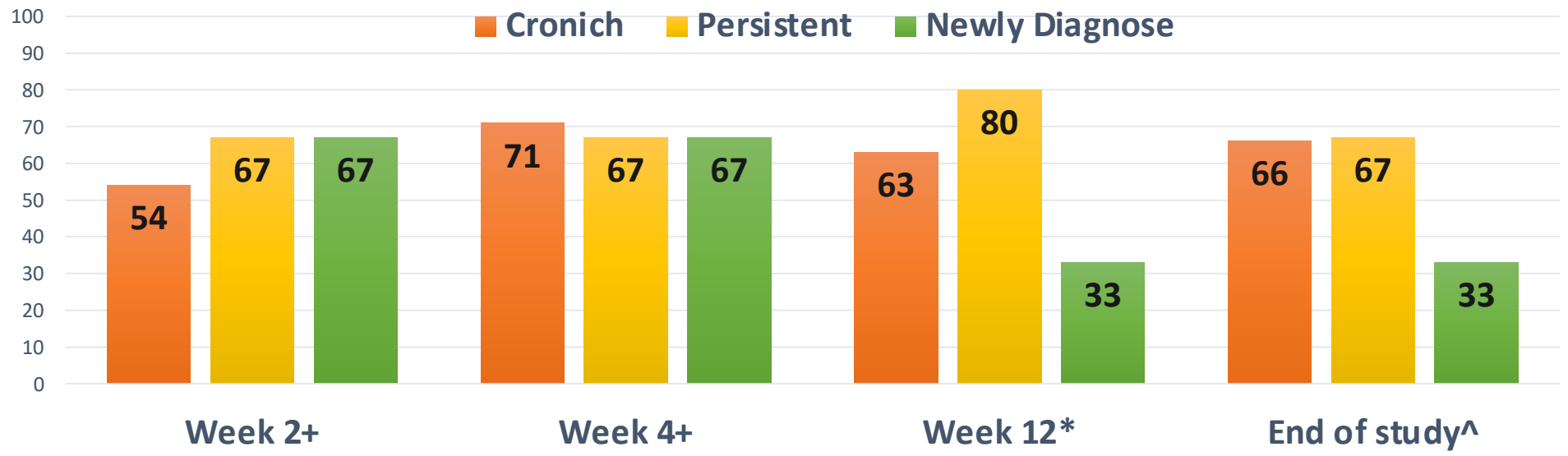


+ 44 patients evaluated
* 40 patients evaluated
^ 40 patients evaluated

Jiménez-Bárcenas R, et al. Br J Haematol. Br J Haematol. 2024 May;204(5):1977-1985.

Real-World Use of Fostamatinib in Andalusia, Spain

Evolution of global response with regard to Type of ITP (%)



+ 44 patients evaluated
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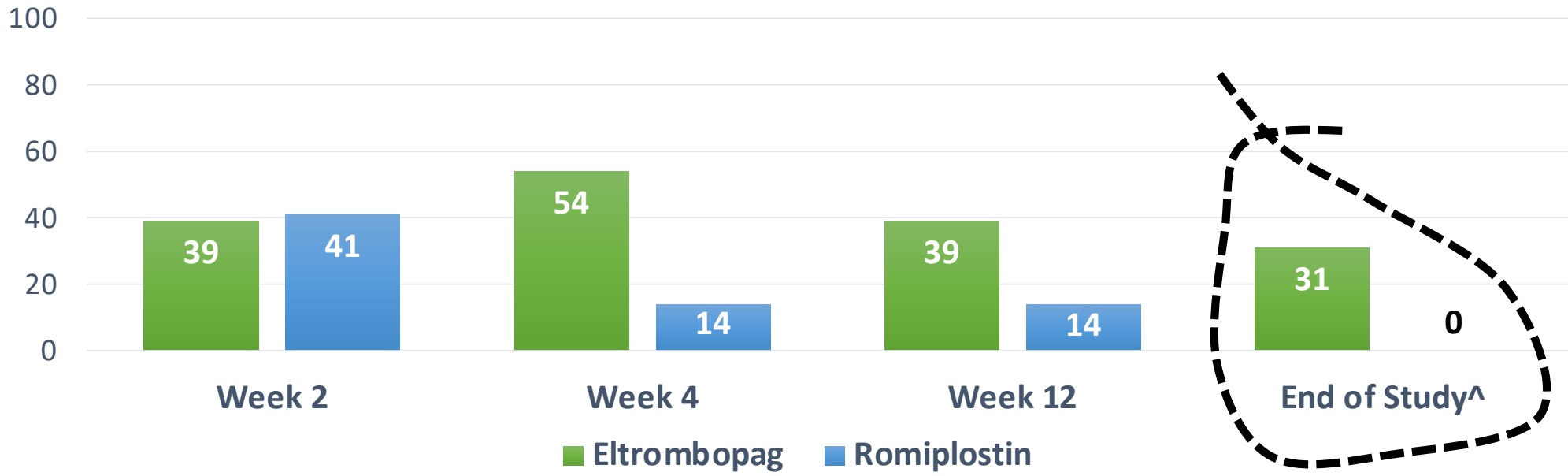
Jiménez-Bárcenas R, et al. Br J Haematol. Br J Haematol. 2024 May;204(5):1977-1985.

Real-World Use of Fostamatinib in Andalusia, Spain

Evolution of response in patients with no satisfactory response to TPO-RA (%)

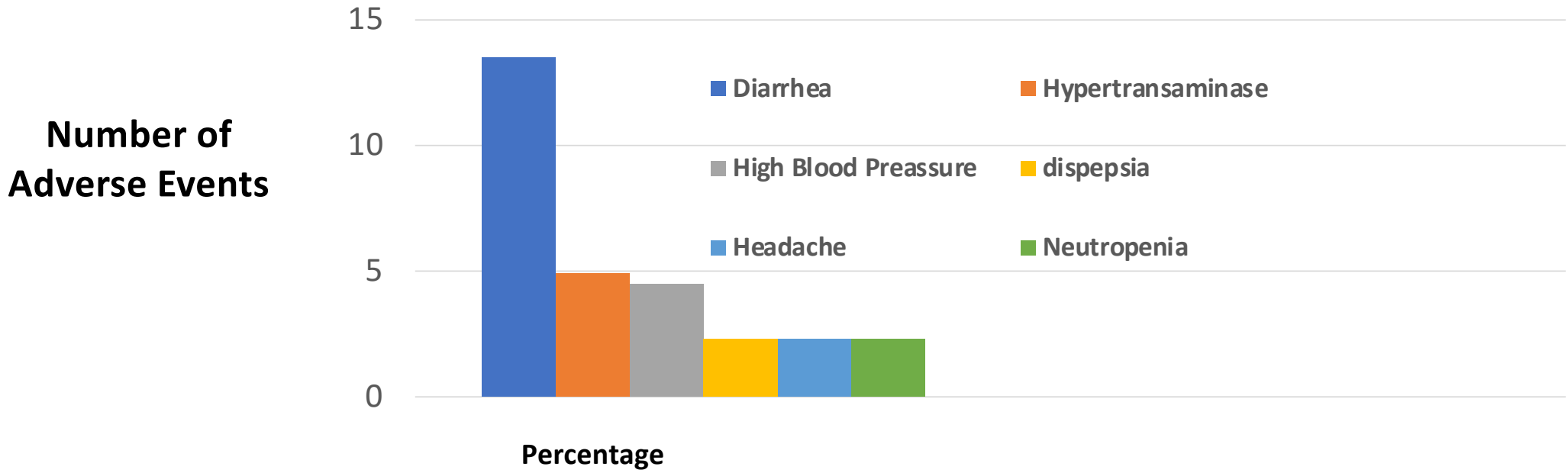


Jiménez-Bárcenas R, et al. Br J Haematol. Br J Haematol. 2024 May;204(5):1977-1985.

Real-World Use of Fostamatinib in Andalusia, Spain

Adverse Events:

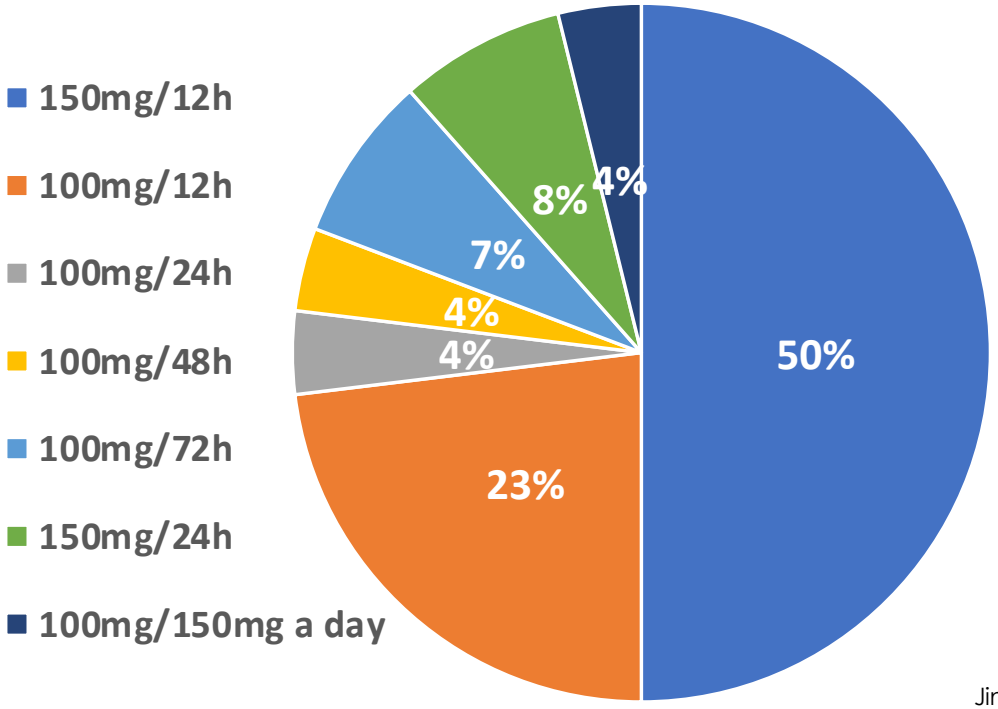
NON STOP OF FOSTAMATINIB



Jiménez-Bárcenas R, et al. Br J Haematol. Br J Haematol. 2024 May;204(5):1977-1985.

Real-World Use of Fostamatinib in Andalusia, Spain

Doses 26 patients still on active treatment with fostamatinib



27% responders associated with other drugs

- Prednisone (n=1)
- Prednisone + immunoglobulin (n=1)
- Dexamethasone + azatioprine (n=1)
- Immunoglobulin (n=2)
- Avatrombopag (n=2)

Jiménez-Bárcenas R, et al. Br J Haematol. Br J Haematol. 2024 May;204(5):1977-1985.

Fostamatinib: Tapering and Sustained Response

150mg/12 h

↓

150mg/100mg a day

↓

100mg/12 h

↓

100mg/24 h

↓

100mg/48 h

↓

100mg twice a week

↓

Discontinue

Tapering:

- Patients under Complete remission
- Patients will be reviewed every 2 weeks
- If platelets above 50x10^9/L after 4 weeks, to to next step

61 patients

↓

13 started tapering

↓

9 discontinue

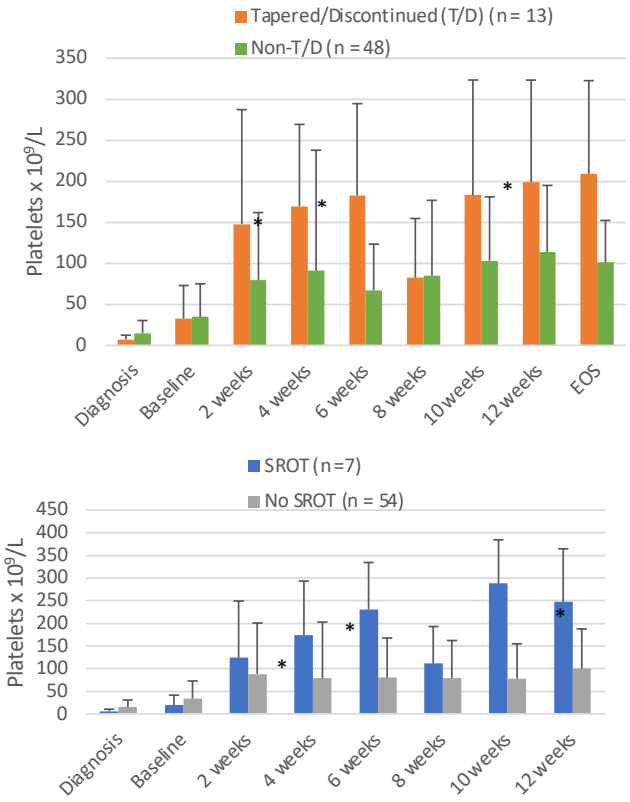
↓

7 SROT

Mingot-Castellano ME, et al. J Clin Med. 2024 Oct 22;13(21):6294. doi: 10.3390/jcm13216294

Fostamatinib: Tapering and Sustained Response

Platelet > 100x10^9/L at week 12, only predictive factors for successful tapering and discontinuation



- **Time to start tapering:** 116 days (IQR: 42-140)
- **Duration of tapering:** 112.5 days (IQR 94.5-191).
- **Median platelet count at tapering:** 232×10^9/L (IQR 152-345×10^9/L)
- **Median platelet count at discontinuation:** 190×10^9/L (IQR 142.5-316.5×10^9/L).
- **Median follow-up since discontinuation**: 263 days (IQR: 247-313 days)
- **Only 2 patients relapsed**
- **Platelet counts higher than 100x10^9/L at week 12 was the only positive predictive** factors for successful tapering and discontinuation.

Mingot-Castellano ME, et al. J Clin Med. 2024 Oct 22;13(21):6294. doi: 10.3390/jcm13216294

Real-World Use of Fostamatinib in the world



	Spain *real-world*	Italy *real-world*	France *real-world*
EHA 2024 presentations	P3323 Gonzalez-Lopez et al	**P2232 e-poster** Lucchini E. et al	**P2245 e-poster** Moulis et al.
Patients	138	91	115
Number of centers	42	20	Carmen registry
Primary ITP	88%	94.5%	87%
Median age	66	63	48
Median months since diagnosis	51	84	60
Median number of prior treatments	**4 (IQR, 2-5)**	**82% ≥3 lines of tx**	**6**
Prior TPO-RA exposure	Elt 76%, Romi 57%	Elt 73%, Romi 57%, Ava 5%	84%
Prior splenectomy	14%	23%	35%
Overall Response **Complete Response**	**79%** **54%**	**72%** **34%**	**80%**
Median months exposure to Fostamatinib		3.7	3.7
Patients in response at month 6		**47%**	
Patients receiving Fostamatinib at: **Month 6** **Month12**		 **40%** **28%**	**> 50% of patients still in tx at the time of the analysis**

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Real-World Use of Fostamatinib in the world

Effectiveness and Safety of Fostamatinib for the Treatment of Immune Thrombocytopenia in Clinical Practice

Context of Research

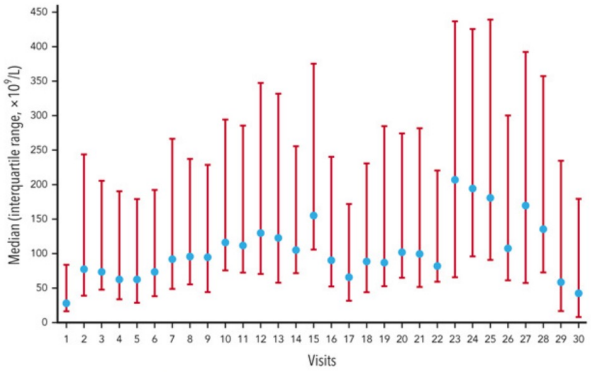
- Fostamatinib is a spleen tyrosine kinase inhibitor approved for the treatment of chronic immune thrombocytopenia (ITP) in patients without adequate response to at least 1 prior line of therapy
- The efficacy and safety of fostamatinib were evaluated in two identical, industry-sponsored, multicenter, randomized, controlled Phase 3 trials (NCT02076399, NCT02076412)
- Limited data are available on the use of fostamatinib in clinical practice

Patients and Methods

- Real-world evidence study
- 138 ITP patients from 42 Spanish centers
- Median age: 66 years
- Median PTL count: 13×10^9/L
- Median no. of previous treatments: 4 (IQR, 2-5)
- Fostamatinib dose: 100 mg BD initially, increased to 150 mg BD if PLT count was inadequate after 4 weeks

Main Findings

- Median treatment duration: 210 days
- Response (PLT count ≥30×10^9/L without any bleeding): 109/138 or 79%



- Discontinuation for lack of efficacy: 27/109 (25%)
- Safety: 67/138 (49%) adverse events (diarrhea, hypertension or neutropenia, mild or moderate)

González-López TJ, et al. Blood. 2024 Aug 8;144(6):646-656.

Variable	n (%)
Any adverse event	94 (100)
Number of grade 3-4 events	13 (13.8)
Diarrhea	28 (29.8)
Hypertension	21 (22.3)
Neutropenia grade 3-4	10 (10.6)
Headaches	8 (8.5)
Hepatobiliary laboratory abnormalities	7 (7.4)
Dyspepsia/epigastralgia	4 (4.25)
Depression	2 (2.1)
Blurred vision/macular lesion	2 (2.1)
Nausea/vertigo	1 (1.06)
Anorexia	1 (1.06)
Asthenia	1 (1.06)
Erythromelalgia	1 (1.06)
Cold sores	1 (1.06)
Hypophosphatemia	1 (1.06)
Pruritus	1 (1.06)
Muscle cramps	1 (1.06)
Mouth sores	1 (1.06)
Myalgia	1 (1.06)
Venous thromboembolism	1 (1.06)
Acute myocardial infarction	1 (1.06)

Real-World Use of Fostamatinib in the world

Variable	Primary ITP (n = 122)	Secondary ITP (n = 16)	Statistical significance (*P* value)
Quality of response			
Patients with a platelet response, n (%)	**98 (80.3%)**	**11 (68.7%)**	.537
Response stratified by variables			
Fostamatinib monotherapy vs use in combination			
Fostamatinib monotherapy	63 (87.5%)	6 (66.7%)	.234
Fostamatinib use in combination	34 (69.4%)	5 (71.4%)	.913
Platelet count at fostamatinib initiation (<20 × 10^9/L vs ≥20 × 10^9/L)			
<20 × 10^9/L	40 (69%)	3 (50%)	.385
≥20 × 10^9/L	55 (90.2%)	8 (80%)	.313
Patients with a complete platelet response, n (%)	**67 (55.4%)**	**7 (43.8%)**	.381
Number of days to platelet response, median (IQR)	**11 (7-21)**	**21 (9-22)**	.044
Number of days to platelet response stratified by variables			
Prior therapy with rituximab			
Yes	21 (14-36)	22 (21-54)	.126
No	9 (7-15)	14 (8-20)	.874
Fostamatinib monotherapy vs use in combination			
Monotherapy	11 (7-19)	21 (11-22)	.438
Combination	14 (8-28)	17 (10-22)	.109

Worse response:

- Combination vs monotherapy
- Platelets <20x10^9/L
- Secundary ITP

González-López TJ, et al. Blood. 2024 Aug 8;144(6):646-656.

Real-World Use of Fostamatinib in the world

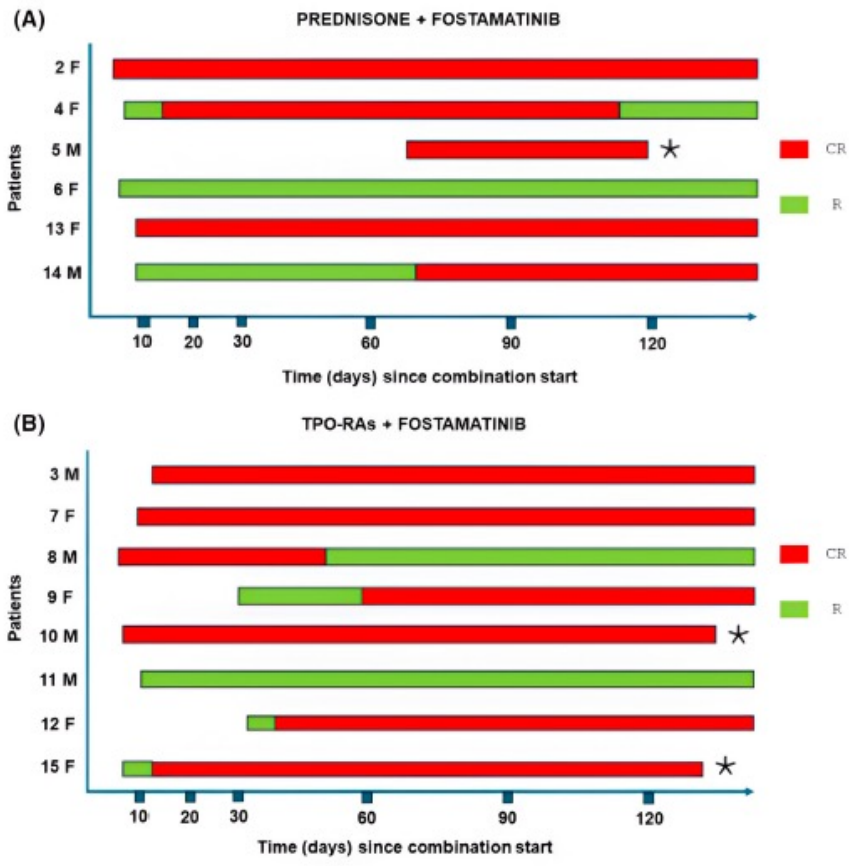
SAFETY INFORMATION

Parameter, *n* (%)	Fostamatinib (*n* = 51)	Eltrombopag (*n* = 87)	Romiplostim (*n* = 127)	Avatrombopag (*n* = 44)
AEs reported during therapy	46 (90.2)	27 (31.0)	53 (41.7)	24 (54.5)
AEs associated with drug discontinuation	4 (7.8)	13 (14.9)	6 (4.7)	5 (11.4)
AEs leading to unplanned clinic visit	1 (2.0)	2 (2.3)	1 (0.8)	2 (4.5)
AEs leading to ER visit	2 (4.0)	1 (1.1)	6 (4.7)	0 (0.0)
AEs leading to hospital visit	5 (9.8)	2 (2.3)	8 (6.3)	0 (0.0)
Type of AE				
Diarrhea	9 (17.6)	4 (4.6)	3 (2.4)	0 (0.0)
Fatigue	6 (11.8)	6 (6.9)	13 (10.2)	5 (11.4)
Headache	5 (9.8)	2 (2.3)	6 (4.7)	4 (9.1)
Nausea	5 (9.8)	2 (2.3)	4 (3.1)	3 (6.8)
Hypertension	4 (7.8)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain	2 (3.9)	1 (1.1)	4 (3.1)	0 (0.0)
Rash	1 (2.0)	1 (1.1)	4 (3.1)	2 (4.5)
Chest pain	1 (2.0)	0 (0.0)	0 (0.0))	0 (0.0)
Neutropenia	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other[1]	12 (23.5)	11 (12.6)	19 (15.0)	10 (22.7)
Thromboembolic events	2 (3.9)	8 (9.2)	6 (4.7)	5 (11.4)

AEs, adverse events; ER, emergency room. [1]These include transaminitis, hematuria, muscle aches, constipation, fluid retention, leg swelling, loss of taste, pancytopenia, dizziness, edema, and vomiting.

Dranitsaris G, et al. Acta Haematol. 2024;147(3):333-343.

Combined therapy Fostamatinib: Italian experience



- Fostamatinib was initially 100 mg BID in all patients
- Need increase dose 40% patients
- 80% Response, median time of 9 days (IQR 7–19)
- 73% Complete response, median time 13 days (IQR 9–39)
- 40% discontinued steroids or TPO-RA, median time of 80 days (IQR 43–142)
- 40% no possible discontinued
- Fostamatinib discontinued:
  - 20% for intolerance
  - 13% relapses

Passucci M, et al. Br J Haematol. 2024 May;204(5):2129-2132

Fostamatinib in combination:
Avatrombopag+Fostamatinib

112 treat with AVA

28 no response to AVA

18 treated with AVA-FOS

- Median age: 60 years-old (IQR: 37-69)
- 78% males.
- Chronic 12, Persistent 5, 1 Newly diagnose
- median 5 lines of treatment (IQR: 4-7).
- Rituximab 4 patients, 12 eltrombopag, 15 romiplostim
- Overall response of the combination was 83.3% (8 CR, 7 R, 3 NR)
- Median time to maximun response of 15 days (IQR: 8-35 days).
- Median dose at response AVA 280mg a week and FOS 2100mg a week.
- Median dose at last visit AVA was 140mg a week and FOS 1400mg a week.

Mingot Castellano ME et al. Br J Haematol. 2024 Oct;205(4):1551-1555.

Fostamatinib in combination: Avatrombopag+Fostamatinib

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 (x10e9/L)	FOS at start combination (mg/week)	Type of Response to AVA-FOS combination	Time to response (days)	Dose of FOS at maximun response (mg/week)	Dose of AVA at maximun response (mg/week)	Relpase	Rescue teatment	Dose of FOS Last visit (mg/week)	AVA at Last visit (mg/week)	Platelets last visit (x10e9/L)
1	Male	40	7	Persistent	5		Yes	Yes	26	2100	CR	21	2100	280	No		1400	80	96
2	Male	60	38	Chronic	8	Yes	Yes	Yes	21	2100	CR	14	2100	280	Yes, during tapering	No	1400	280	74
3	Male	69	48	Chronic	8	Yes	Yes	Yes	14	2100	CR	8	2100	280	No		2100	140	52
4	Male	34	12	Chronic	7	Yes	Yes	Yes	12	2100	R	13	2100	28	No		2100	140	54
5	Male	69	50	Chronic	4		No	Yes	11	1400	CR	14	1400	0	No		700	60	98
6	Male	63	59	Chronic	7	Yes	Yes	Yes	13	2100	R	84	2100	280	No		1400	140	44
7	Male	50	10	Persistent	6		Yes	Yes	18	1400	CR	25	1400	280	No		700	80	74
8	Female	76	19	Chronic	4		Yes	Yes	5	2100	NR	n.a.	n.a.	n.a.	n.a.		n.a.	n.a.	n.a.
9	Male	60	2.3	Newly diagnose	3		No	No	21	2100	NR	n.a.	n.a.	n.a.	n.a.		n.a.	n.a.	n.a.
10	Female	16	17	Chronic	3		Yes	Yes	25	2100	R	69	2100	280	Yes, during tapering	Immunoglobulin	1400	140	42
11	Male	59	28	Chronic	5		Yes	Yes	8	2100	NR	n.a.	n.a.	n.a.	n.a.		n.a.	n.a.	n.a.
12	Male	85	10	Persistent	4		No	No	10	2100	R	14	2100	140	No		2100	280	65
13	Female	74	72	Chronic	7		Yes	Yes	13	1400	CR	8	1400	280	No		1400	280	329
14	Female	30	56	Chronic	4		Yes	Yes	10	1400	CR	8	1400	140	Yes, during tapering	Dexamethasone	1400	80	107
15	Male	61	8	Persistent	4		No	Yes	21	1400	R	78	1400	28	No		1400	280	176
16	Male	28	4	Persistent	4		No	Yes	9	2100	R	70	2100	280	Yes, during tapering	No	1400	280	122
17	Male	86	15	Chronic	4		Yes	No	15	2100	CR	21	2100	140	No		2100	140	106
18	Male	28	28	Chronic	5		No	Yes	18	2100	R	16	2100	280	No		2100	280	145

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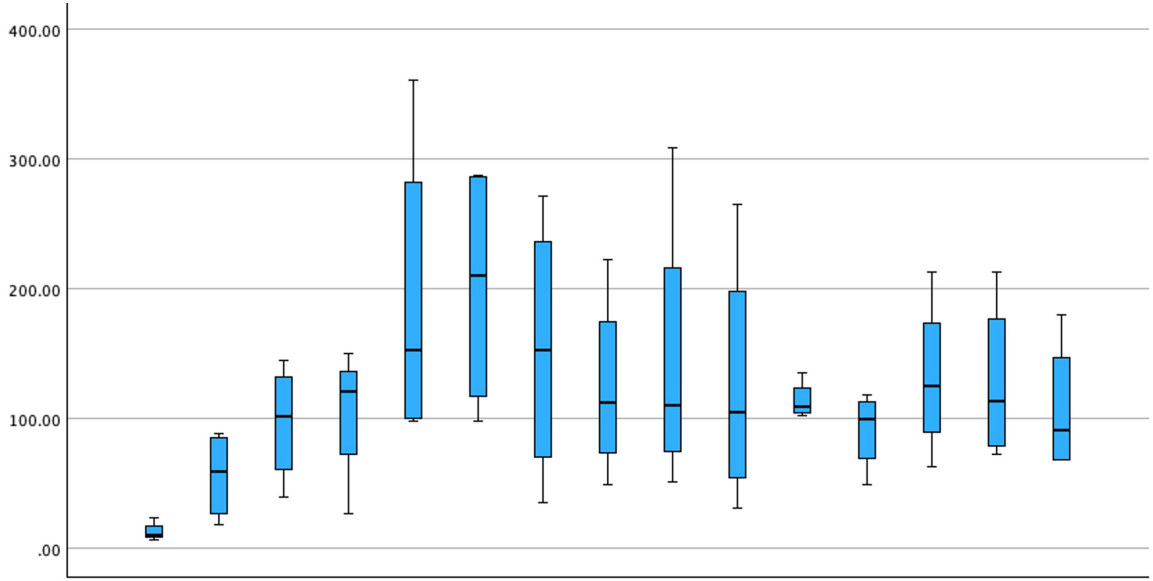
Fostamatinib in combination: Avatrombopag+Fostamatinib



	Basal	WeeK2	WeeK4	Week8	Week12	Week16	Week18	Week22	Week26	Week30	Week34	Week38	Week42	Week46	Week48
Patients (n)	15	15	15	15	15	15	14	12	10	8	7	6	4	4	4
Respose (CR) Complete	0	0	6	8	7	5	6	5	4	4	6	3	3	2	2
Response (R)	0	9	9	2	7	10	8	7	6	3	1	3	1	2	2
Platelet count fraction on response		0.6	1	0.67	0.93	1	1	1	1	0.88	1	1	1	1	1

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Fostamatinib in combination: Avatrombopag+Fostamatinib

112 treat with AVA

↓

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↓

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33%AEs

AVATROMBOPAG:

- Headache 1 patient
- WHO grade 2 liver in 1 patient which was solved after the interruption of AVA for 6 days and reintroduction at a lower dose, from 140mg to 60mg weekly.

FOSTAMATINIB:

- Diarrhoea grade 1 was communicated in 3 patients
- Neutropenia grade 3 in 2 patient

No vascular event or infection

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Take-home messages

- Fostamatinib 2nd line ITP, alternative to TPO-RA (different mechanism of action)
- Fostamatinib is an effective and safe drug in ITP
- Efficacy improves with earlier use and side effects are easily controlled and managed
- Combination of TPO-Ra and immunossuppresive therapy could be a good option of refractory ITP
- Questions to answer with evidence:

  - What dose to start with?
  - Which is the best scheme to do transition from other 2º lines treatments?
  - Tapering with fostamatinib?
  - Special populations: Vascular risk, …

Instituto de Biomedicina de Sevilla

Servicio de Hematología
Hospital Universitario Virgen del Rocío

mariae.mingot.sspa@juntadeandalucia.es