

Treatment challenges in complicated patients with ITP

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Case: Refractory ITP

- A 56-year woman case to office with history of progressive cutaneous lesions in the last 1 week ago.
- Negative PMH,DH
- She didn't have any evidence of active bleeding in the physical examination
- The initial CBC count:
WBC=7000(N=80%, L=20) /Hb=13/ Plt=2000



- After diagnostic interventions (PBS, R/O of secondary causes and BMA), treatment with corticosteroid was initiated.
- After 3 days plt count didn't rise and IVIG started but plt count remained <10,000
- What is the next step?

Refractory ITP

- Definition:

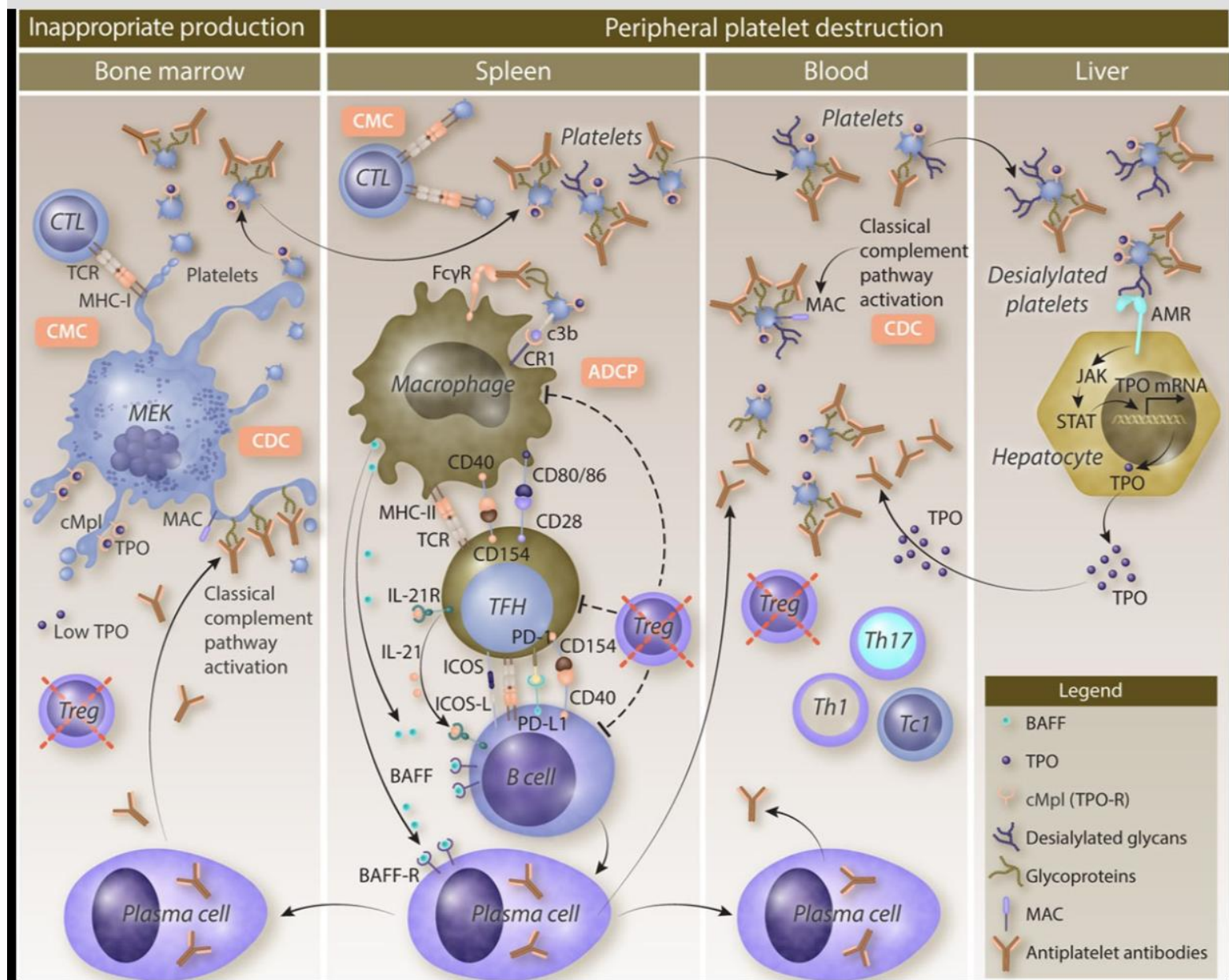
No universally accepted definition

Commonly used criteria:

- Failure of ≥ 2 lines of therapy or
- Persistent severe thrombocytopenia with bleeding risk.

Pathophysiology of Refractoriness

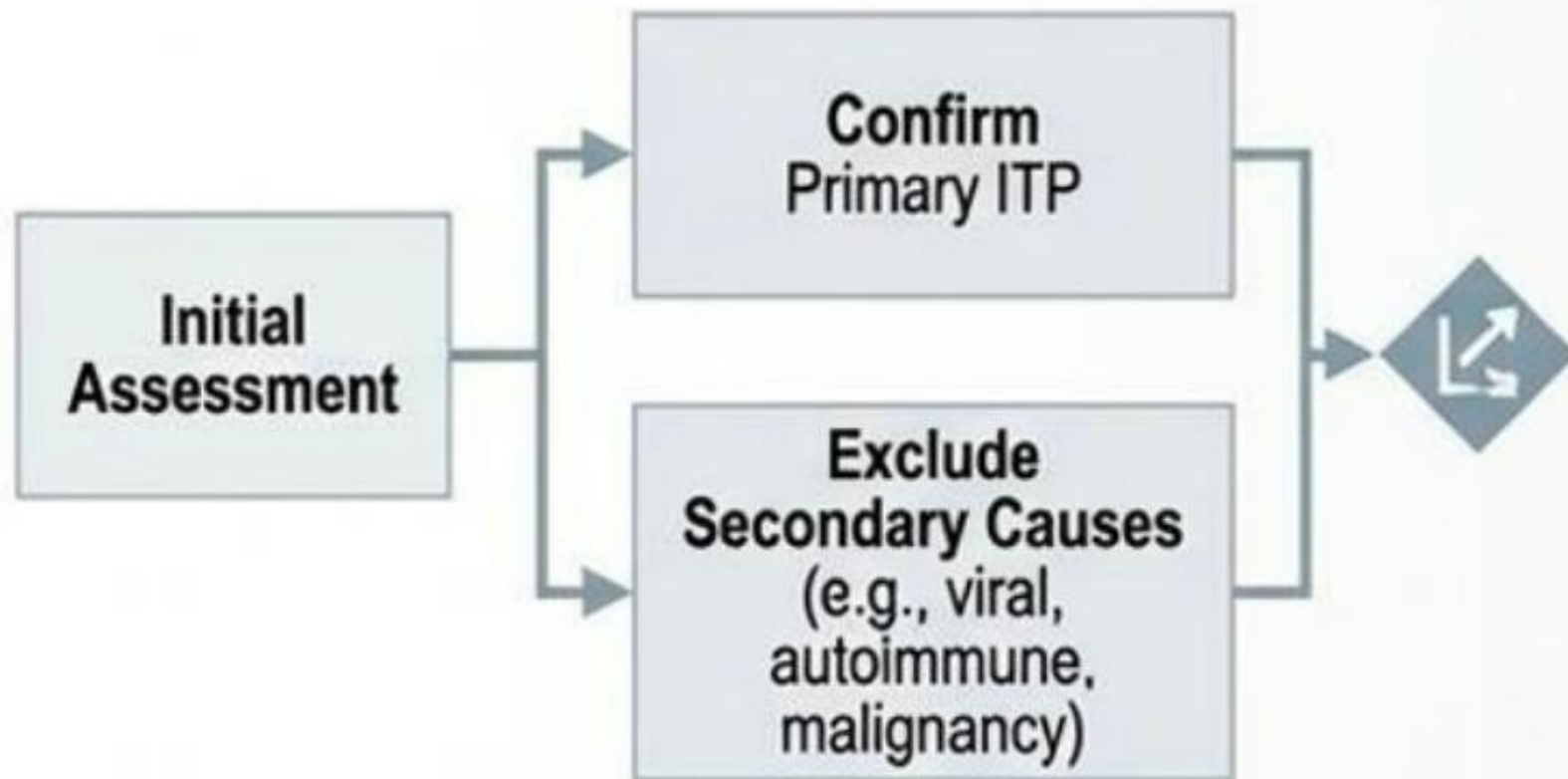
- Persistent autoantibody production
- Cytotoxic T-cell–mediated platelet destruction
- Impaired megakaryopoiesis
- Loss of response to immune modulation over time



Mechanism	Key Pathways
Peripheral Destruction	<ul style="list-style-type: none"> - Autoantibody-mediated (FcγR) - Complement activation (C3b, MAC) - CTL-mediated cytotoxicity
Impaired Production	<ul style="list-style-type: none"> - TPO mRNA dysregulation - Megakaryocyte apoptosis - Abnormal glycosylation
Immune Dysregulation	<ul style="list-style-type: none"> - Treg/Th17 imbalance - BAFF overproduction - PD-1/PD-L1 dysfunction
Splenic Clearance	<ul style="list-style-type: none"> - Enhanced macrophage activity - Desialylated platelet removal

Treatment considerations

- Confirm the diagnosis
- evaluate for treatable causes of secondary ITP (inherited thrombocytopenia, myelodysplastic syndrome, secondary viral infections or drug-induced thrombocytopenia)
- Often initiate second line therapy at a slightly lower platelet count (<20,000).
- provide appropriate vaccinations prior to immunosuppressive therapy.



Second line treatment

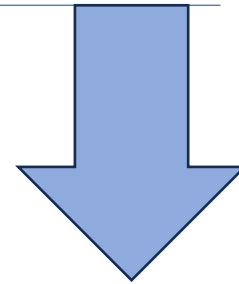
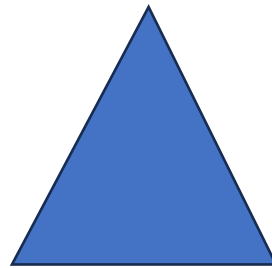
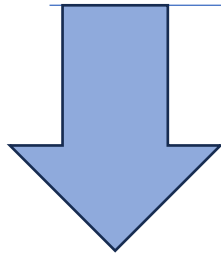
Balancing bleeding risk vs treatment toxicity



bleeding risk

VS.

treatment toxicity



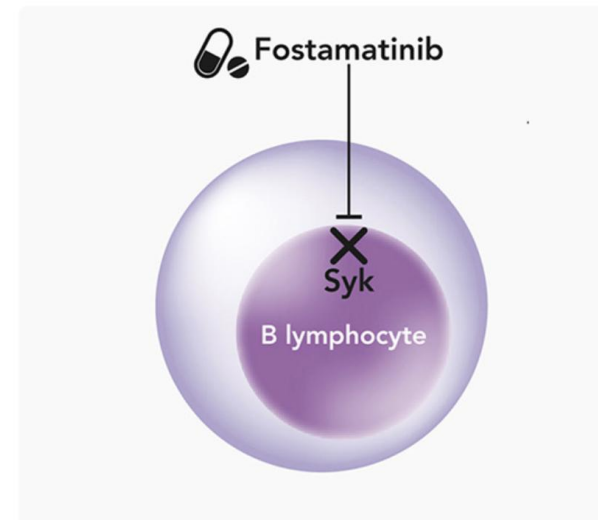
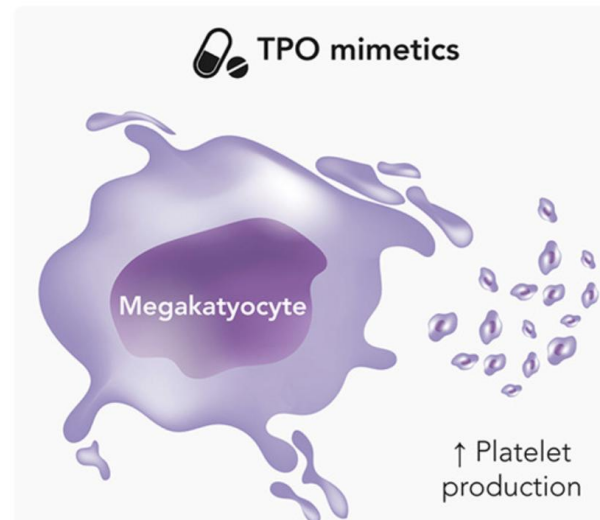
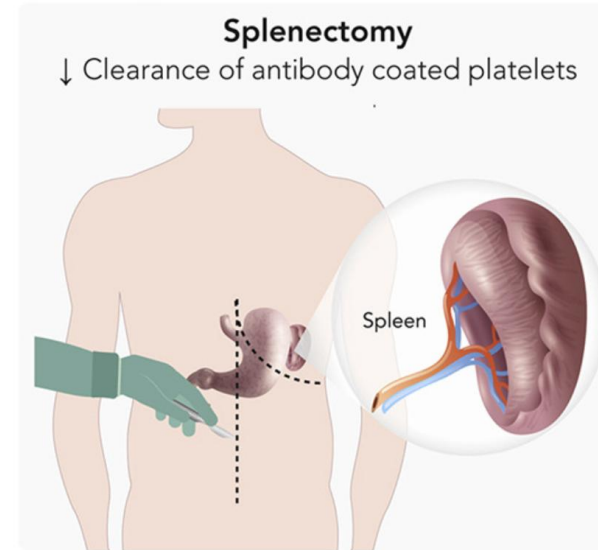
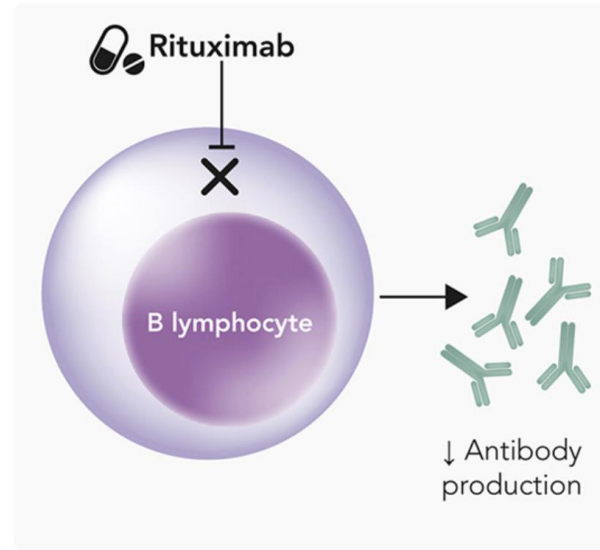
Medical Therapies

- TPO receptor agonists (eltrombopag, romiplostim)
- Immunosuppressants:
 - Rituximab
 - Mycophenolate
 - Azathioprine
 - Cyclosporine
- Fostamatinib (SYK inhibition)

Procedural





- Splenectomy (select cases)

Treatments for refractory ITP



Therapy	Response rate	Time to response	Toxicity	Duration of response
Splenectomy	80% overall, 66% stable	1-24 d	Surgical complications Infection (2-3 times baseline risk) Thrombosis (~2 times baseline risk)	Approximately 2/3 of patients will require no further therapy
Rituximab	60% overall, 40% stable	1-8 wk	Hypersensitivity reactions Immune suppression Hepatitis B reactivation	20-25% sustained at 5 y, although patients may be retreated
TPO mimetics (eg, romiplostim, eltrombopag)	>80% overall, 40-50% stable	2-3 wk	Rebound thrombocytopenia Thrombosis Hepatotoxicity (eltrombopag) Increased marrow reticulin deposition (1.8-7%)	Continuous as long as drug is administered In patients who have an initial response, >90% maintain that response at 5 y
Syk inhibitor (fostamatinib)	43% overall, 18% stable	2-8 wk	Diarrhea, nausea Hypertension Neutropenia	Unknown, but assumed to be continuous as long as drug is administered

Refractory ITP Treatment Landscape: Comparative Analysis of Response & Risk.

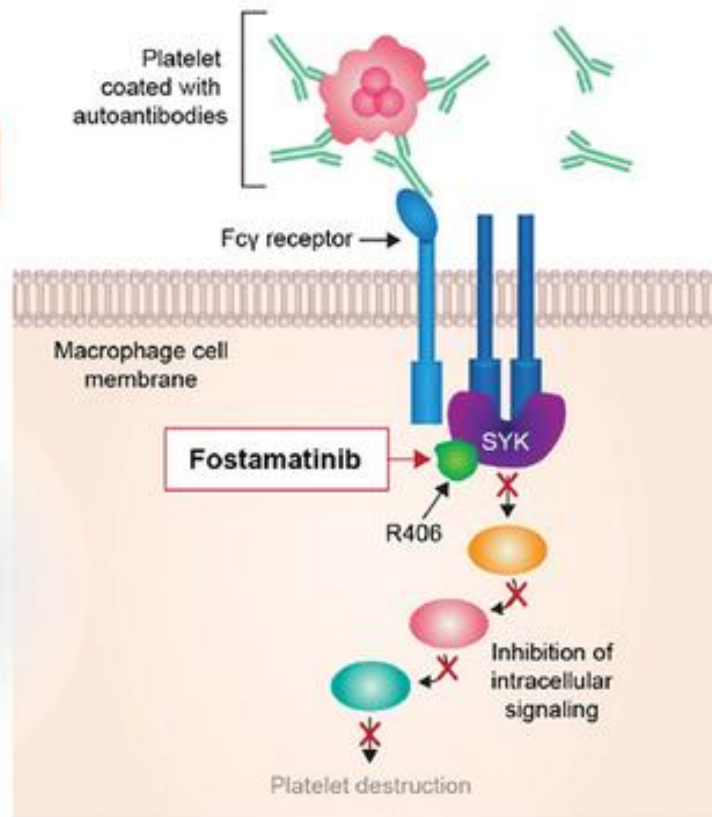
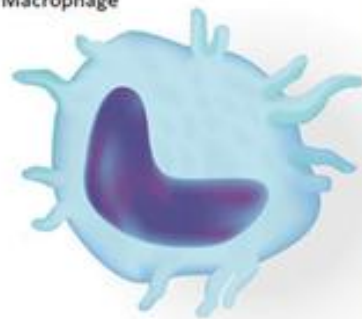
Treatment	Overall Response	Durable / Sustained Response	Key Considerations & Risks
Splenectomy	 80%	66% (Durable)	Surgical & Thrombotic Risk
Rituximab	 60%	20–25% (Sustained at 5 yrs)	Lower Long-Term Efficacy
TPO Mimetics	 >80%	90% (5-yr Maintenance on drug)	Requires Ongoing Therapy
Fostamatinib	 43%	Shorter Follow-up	Limited Long-Term Data



Insight: TPO mimetics offer high sustained response rates with continuous use, while splenectomy provides durable off-treatment response but carries procedure-related risks.

**Fostamatinib
inhibits SYK**

Macrophage





- Our patient's thrombocytopenia was refractory to:
-rituximab, cyclophosphamide, cyclosporin, azathioprine, vincristine,
Romiplostim and Eltrombopag
- What about splenectomy?

- splenectomy has the greatest chance of altering the disease course and resulting in a sustained remission
- The only clinical parameter that predicts a favorable response to splenectomy is patient younger age
- correlation between response to intravenous immune globulin (IVIG) and response to splenectomy?




Platelet threshold for splenectomy???

Gastrointestinal

Laparoscopic Splenectomy for Patients with Immune Thrombocytopenia and Very Low Platelet Count: Is Platelet Transfusion Necessary?

Xiaodong Chen M.D., Ph.D. *, Bing Peng M.D., Ph.D. †  , Yunqiang Cai M.D. †, Jin Zhou M.D. *, Yichao Wang M.D. †, Zhong Wu M.D. †, Sirui Chen M.D. †

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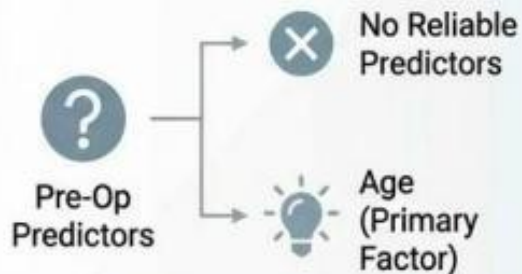
Background

The safe level of platelet count (PC) and necessity for platelet transfusion during laparoscopic splenectomy (LS) remain uncertain in patients with immune thrombocytopenia (ITP).

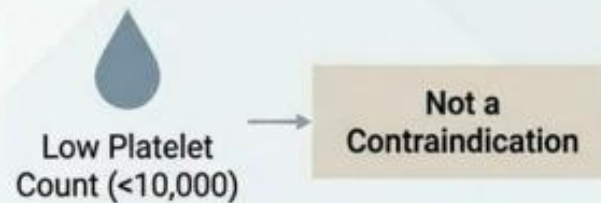
Platelet group ($\times 10^9/L$)	Number of patients	Platelet transfusion	Laparoscopic completion	Blood loss / operative time	Bleeding complications	Key findings
<10	22	6 yes / 16 no	High success rate	Comparable to other groups	No increase	Very low platelets no contraindication; tran not essential
10–30	22	None	High success rate	Comparable	Low	Safe and effective with transfusion
>30	25	None	Highest success rate	Comparable / lowest	Minimal	Reference group with expected outcomes

Splenectomy: Highest Probability of Long-Term Remission.

Efficacy & Prediction



Addressing Low Platelet Counts





Key Considerations

- Highest long-term remission rates.
- Lack of pre-op predictors beyond age.
- Laparoscopic approach enhances viability even with very low counts.


Strategic option for managing refractory ITP with careful peri-operative planning.

Original Article

A multicenter retrospective analysis on therapeutic plasma exchange in immune thrombocytopenic purpura

Abdulkadir Basturk ^a  , Serhat Sayin ^b, Mehmet Ali Erkurt ^c, Ahmet Sarici ^c, Omer Ekinci ^d, Asli Kum ^e, Ilhami Berber ^c, Serdal Korkmaz ^e, Ali Dogan ^f, Turgay Ulas ^g, Irfan Kuku ^c, Bulent Eser ^h, Fevzi Altuntas ⁱ

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After TPE, partial response was achieved in 7 patients (41 %) complete response was achieved in 9 patients (52 %).

Feature	Details
Study type	Multicenter retrospective analysis
Year	2021
Journal	<i>Transfusion and Apheresis Science</i>
Patient population	17 adult patients with refractory ITP (failed steroids, IVIG, or other therapies)
Intervention	Therapeutic plasma exchange (TPE) to remove circulating platelet autoantibodies
Indications	<ul style="list-style-type: none"> - Refractory ITP - Severe symptomatic thrombocytopenia - Pre-surgery platelet optimization when other treatments failed
Mechanism	Physical removal of pathogenic autoantibodies responsible for platelet destruction
Outcomes	<ul style="list-style-type: none"> - TPE led to temporary platelet improvement in most patients - Used as a salvage therapy rather than first-line - No major TPE-related complications reported
Limitations	Small sample size (n=17), retrospective design, lack of long-term follow-up
Clinical takeaway	TPE is not standard first- or second-line therapy in ITP; can be considered in refractory or high-risk cases under specialist supervision

Platelet was $<10,000$ after splenectomy!



Danazole



Danazol is an attenuated androgen with immunomodulator effect. Response rates vary widely—from 10% to 70%—between studies.

AND our patient responded well to this traditional drug! (plt=50,000)

Emerging and Investigational Therapies

- FcRn inhibitors (Efgartigimod,...)
- BTK inhibitors
- Combination therapies
- Personalized treatment approaches
- Ongoing clinical trials

Thanks for your attention

