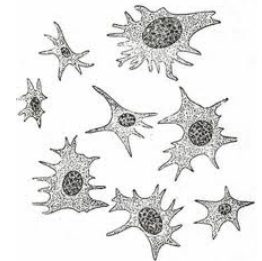


Overview of ITP

Dr Gary Benson

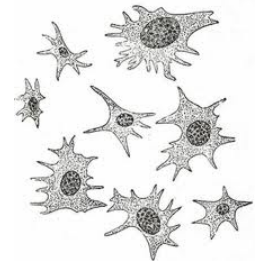
Director N Ireland Haemophilia Comprehensive Care Centre
and Thrombosis Centre

Belfast City Hospital



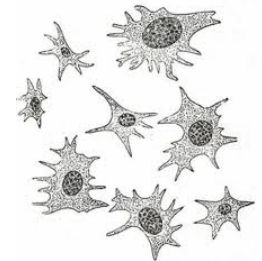
Idiopathic (Immune) Thrombocytopenic Purpura

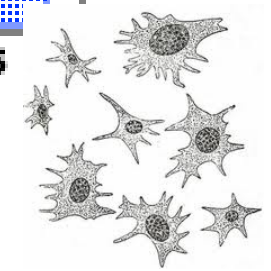
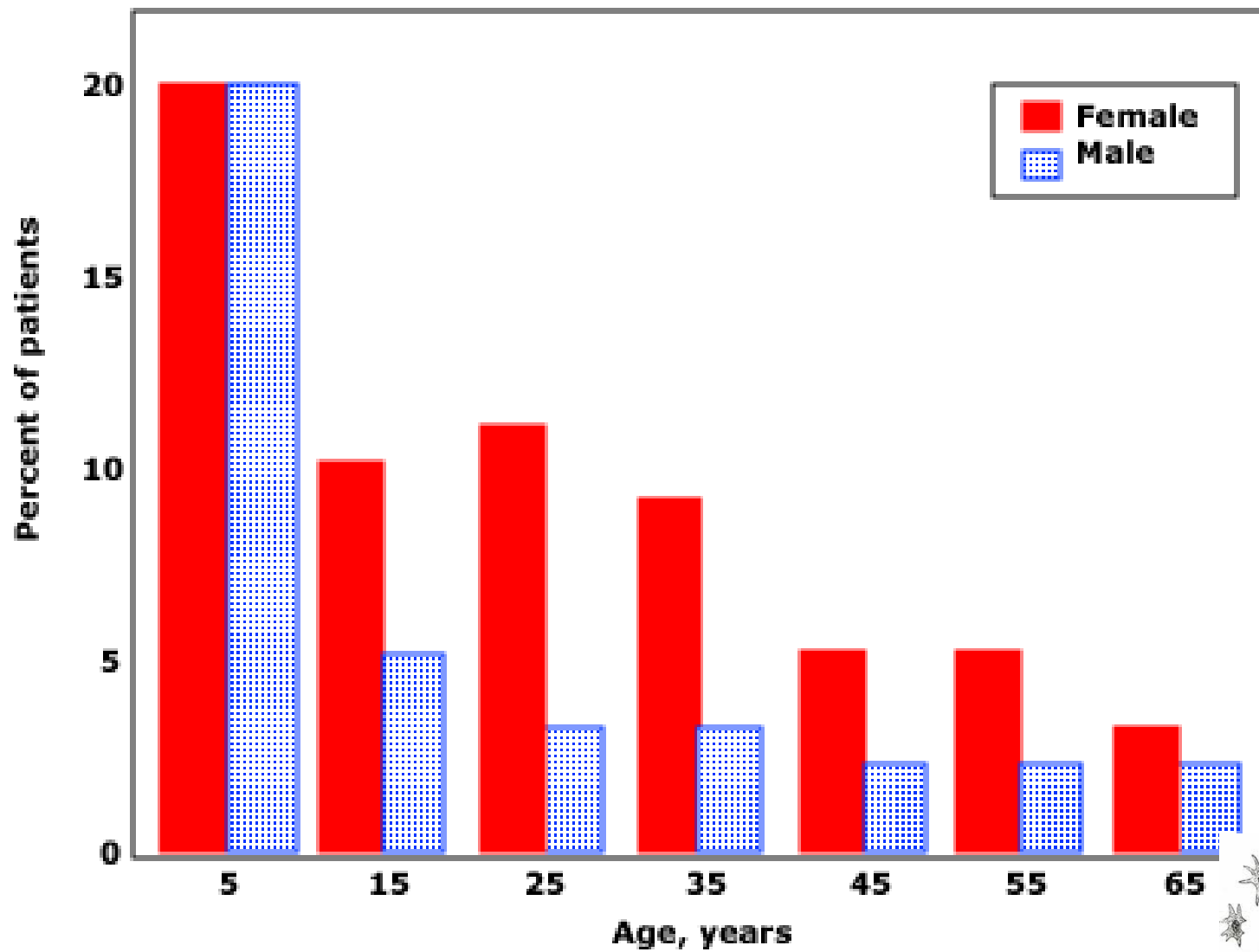
- Thrombocytopenia in the absence of other blood cell abnormalities (normal RBC & WBC, normal blood film)
- No clinically apparent conditions or medications that can account for thrombocytopenia



Statistics of ITP

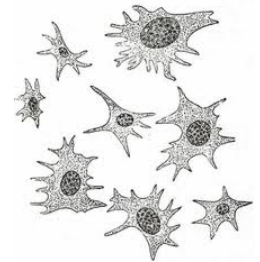
- Incidence of 22 /million/year in one study
- Prevalence greater as often **chronic**
 - *Segal et al → 100 /million/year
 - *age-adjusted prevalence 9.5/100,000
 - *1.9 :1 females / males

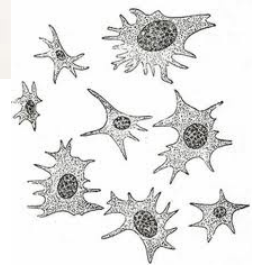


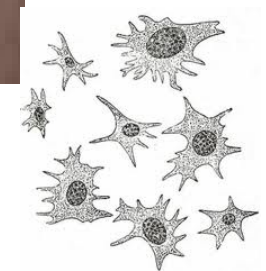


Clinical Manifestations

- May be acute or insidious onset
- **Mucocutaneous Bleeding**
 - *petechiae, purpura, ecchymosis
 - *epistaxis, gum bleeding
 - *menorrhagia
 - ***GI bleed, CNS bleed = RARE**

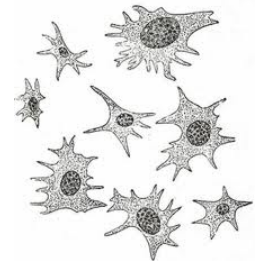






Aetiology of ITP : Children

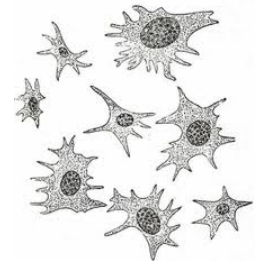
- Maternal associated
- Often after **infection** (viral or bacterial)
 - Post MMR vaccination
- Theories:
 - *antibody cross-reactivity
 - **H. pylori*
 - *bacterial lipopolysaccharides



Aetiology of ITP : Adults

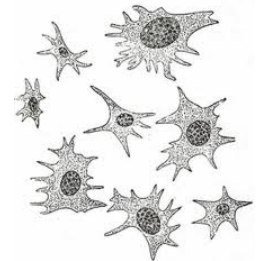


- ?? Auto-antibodies?



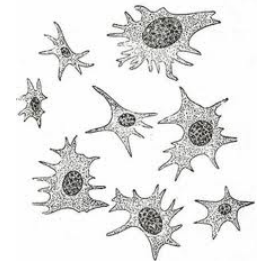
Diagnosis (*of Exclusion*)

- Rule out other causes:
 - *lab error / PLT clumping
 - *drug / medication interaction
 - *infections (HIV, Hepatitis C)
 - *thyroid / autoimmune disease
 - *destructive / consumptive processes (TTP/HUS)
 - *bone marrow disease (leukemias, MDS)



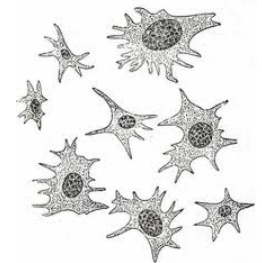
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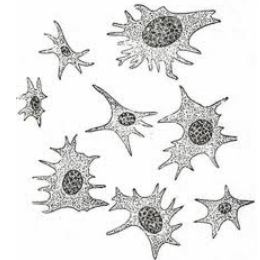
To Marrow or Not to Marrow?

- Bone marrow aspiration & biopsy if...
- Patient 60 yrs. or older
- Poorly responsive to tx
- Unclear clinical picture



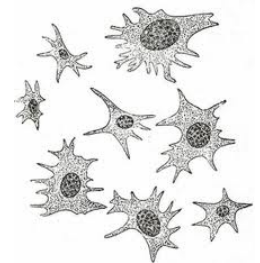
Anti-Platelet Antibody Testing

- **NOT recommended by BSH Practice Guidelines**
- Poor positive/negative predictive values, poor sensitivity with all current testing methods...
- ...and doesn't change the management!



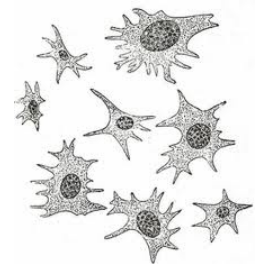
Management of ITP in Adults

- Emergency vs. Chronic Tx
- Goal = prevention of bleeding, NOT cure!



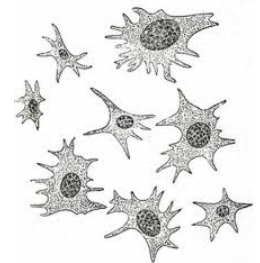
Management of ITP in Adults

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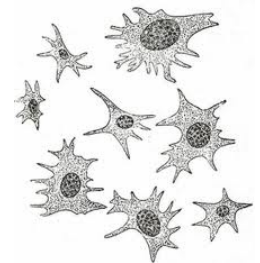
General Principles of Therapy

- Major bleeding **rare** if $PLT > 10,000$
- Goal = get PLT count to safe level to prevent bleeding...
- ...**not** to specifically cure the ITP!



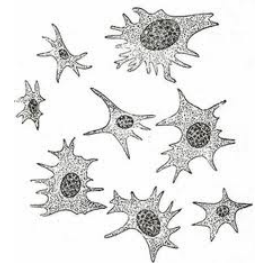
“Safe” Platelet Counts

- “moderately” t-penic = 30-50,000
- Probably safe if asymptomatic
- Caution with elderly (CNS bleeds)



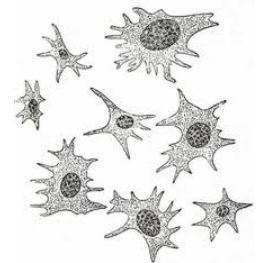
When Planning Therapy...

- Tailor therapy and decision to treat to the individual patient
- Weigh bleeding vs. therapy risks



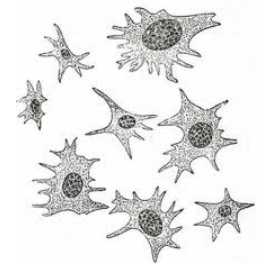
Initial Therapy

- **Prednisolone 1 mg/kg/day**
*usual response within 2 weeks
- Taper off after PLT response
- **Duration** of use = controversial



Second-Line Therapy

- IV Immune Globulin (IVIg)
1 gram/kg/day x 2 days
- anti-D – if pt is Rh+
50-75 mcg/kg/day



Treatment Side-Effects

- Steroids

- *bone density loss

- *muscle weakness

- *GI effects

- *weight gain

- IVIG/anti-D

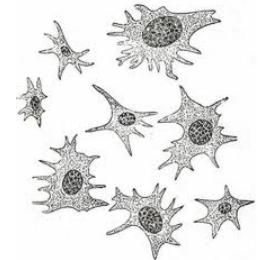
- *hypersensitivity

 - *headache

- *renal failure

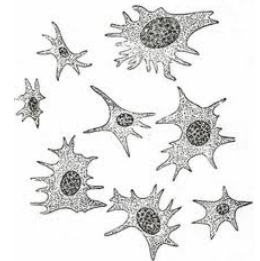
- *nausea/vomiting

- *alloimmune haemolysis



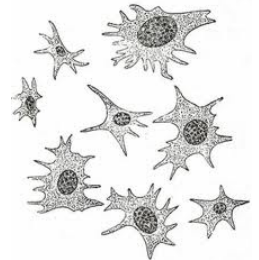
Splenectomy

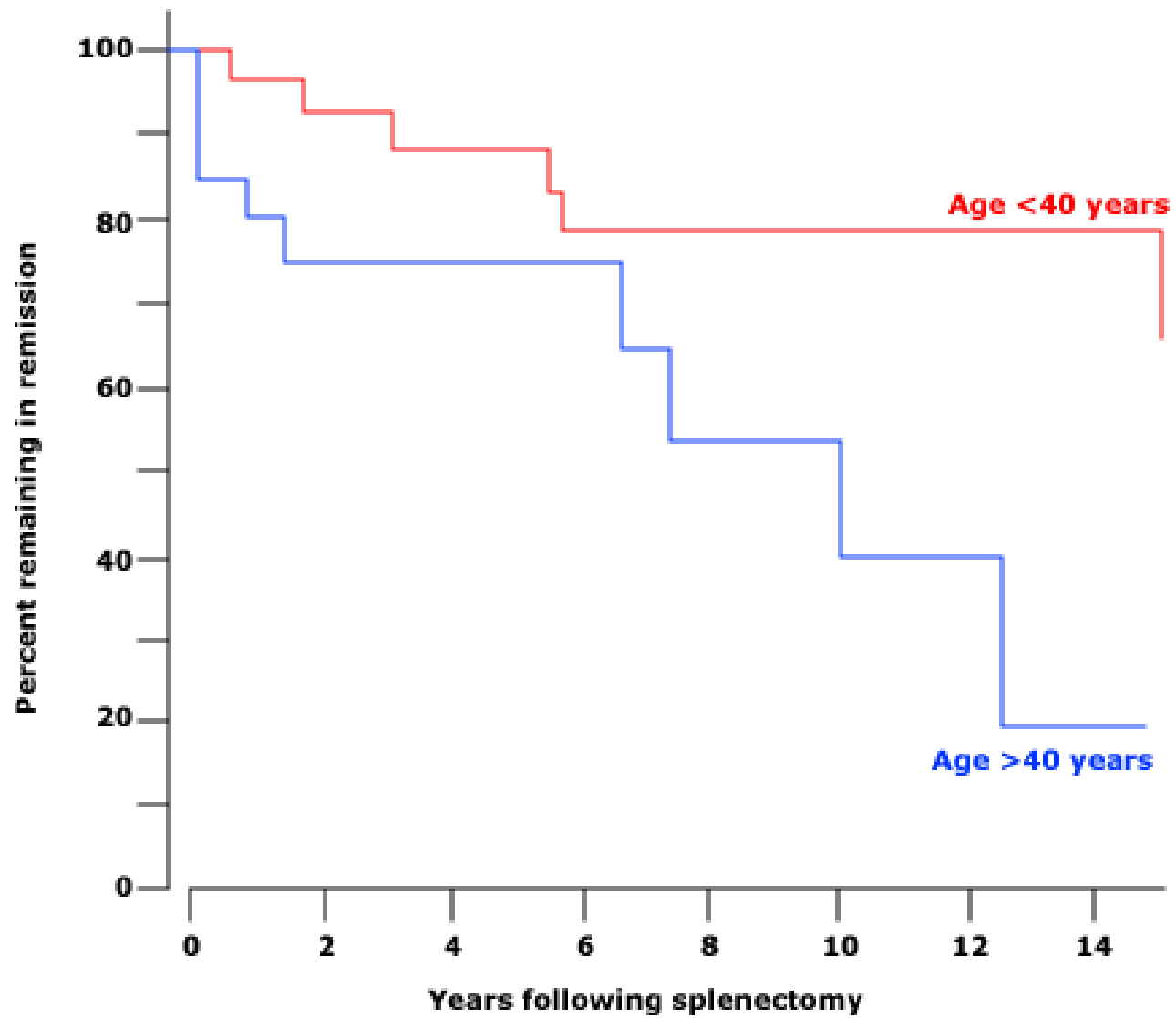
- Usually reserved for treatment failure
- Consider risk of bleeding, pt lifestyle
- **RISKS**
 - *surgical procedure
 - *loss of immune function → vaccinations



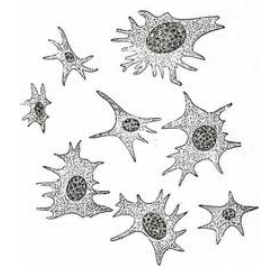
Response Post-Splenectomy

- Usually normalized PLTs within 2 weeks (often immediately)
- Younger pts do better
- Kojouri et al (*Blood* 2004) → 65% CR



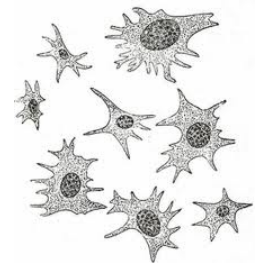


Data from Fabris, F, et al. *Br J Haematol* 2001; 112:637.



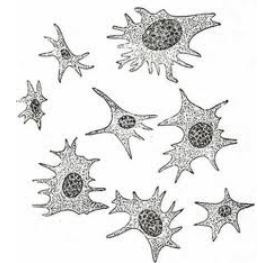
Chronic Refractory ITP

- Persistent > 3 months
- PLT < 50,000
- Failure to respond to splenectomy

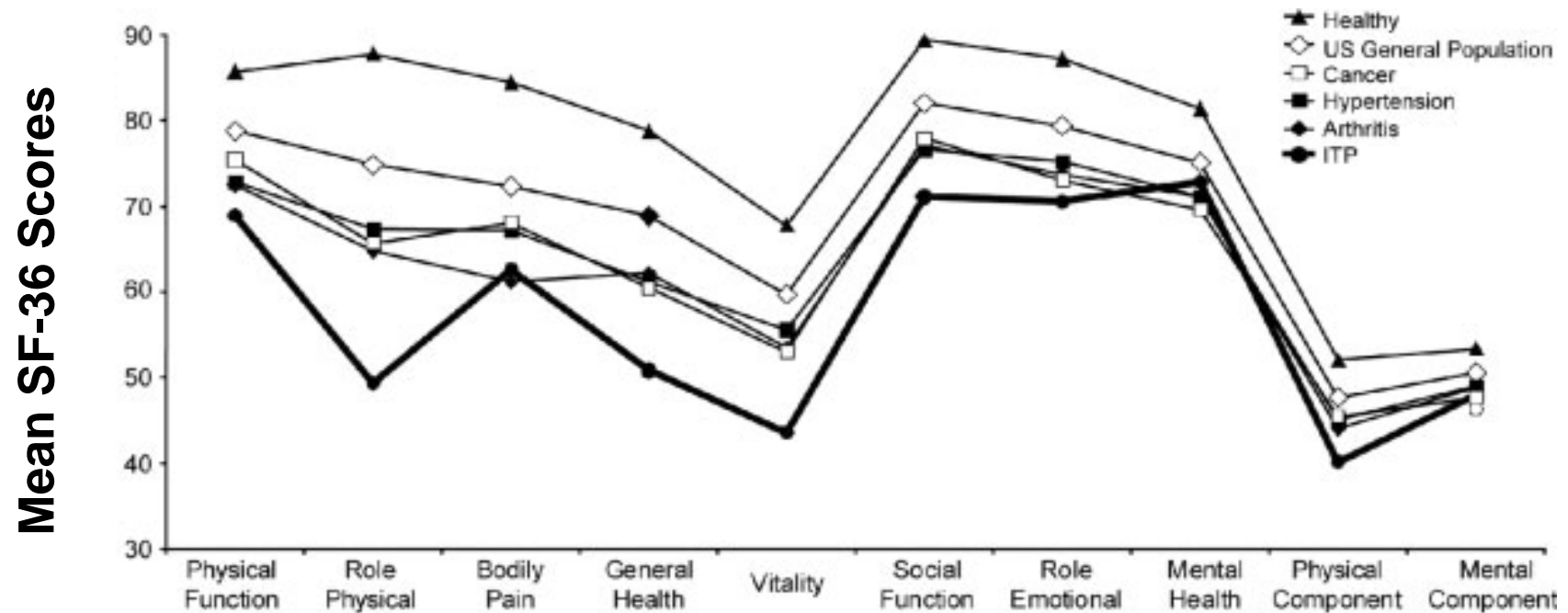


When all else fails...

- Steroids
- IVIg / anti-D
- Rituximab (anti-CD20)
- Cyclophosphamide
- Danazol
- Accessory splenectomy
- *H. pylori* eradication



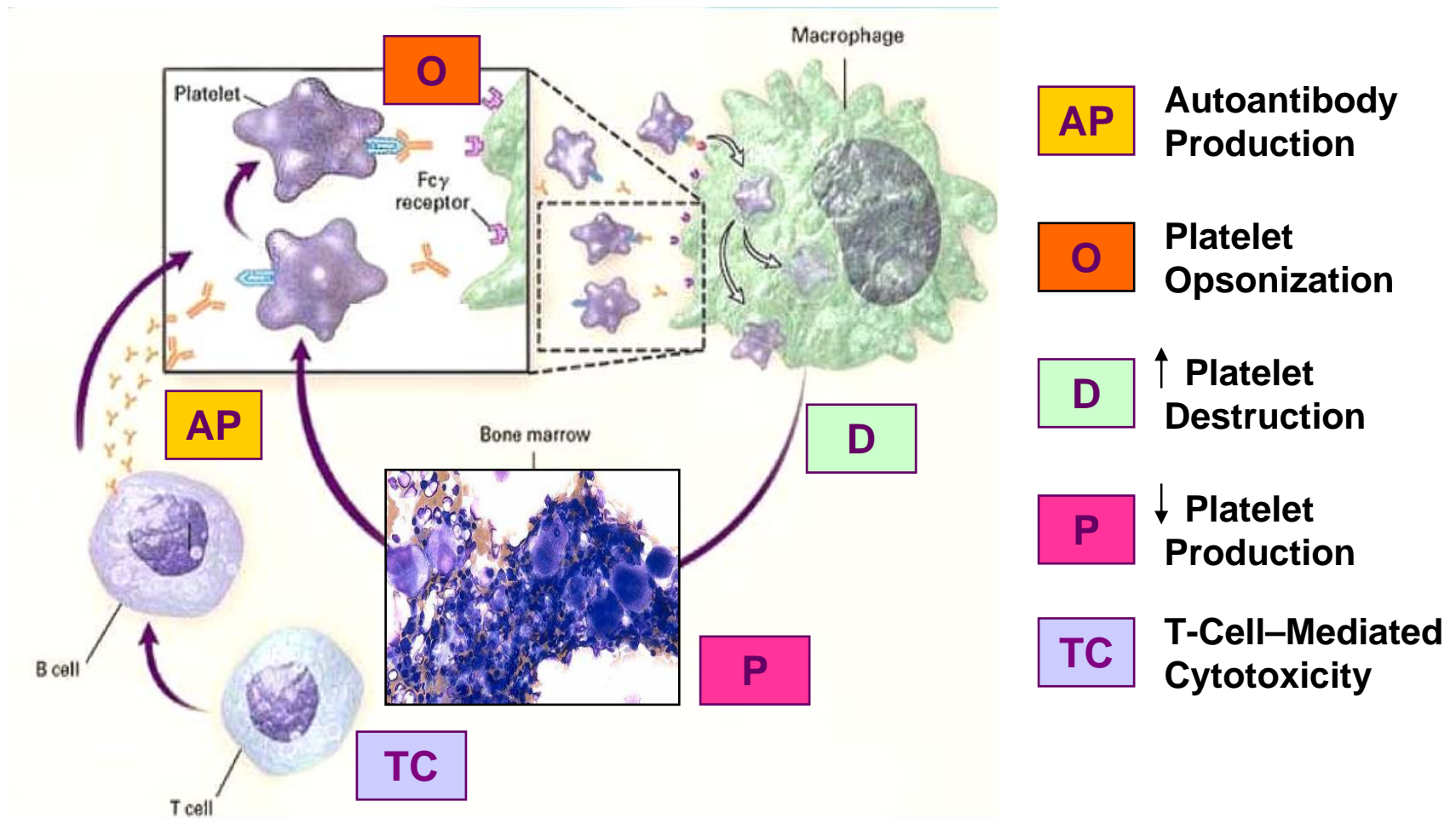
ITP and Health-Related QOL



SF-36 Domains and Component Summary Scales

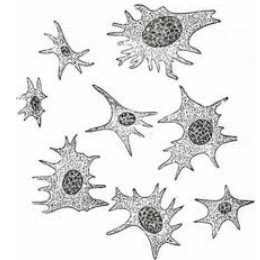
- Patients with ITP have worse QOL than the general population and patients with common disorders
- ITP QOL is better than CHF or missing or paralyzed limb

Pathophysiology of ITP

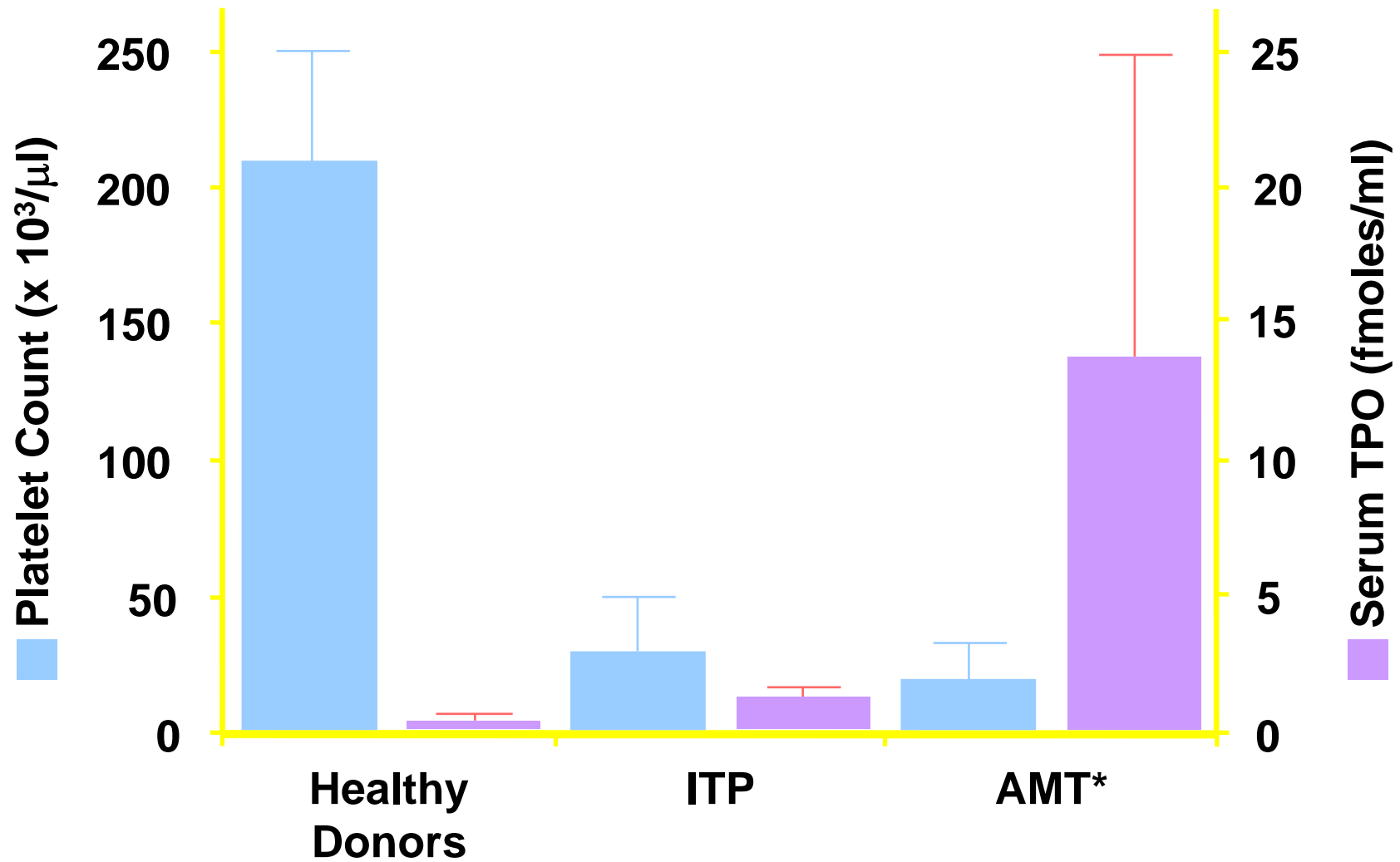


Mechanism-Based Approaches to Treatment

- Inhibit phagocyte-mediated clearance of Ab-coated platelets
 - Steroids
 - Splenectomy
 - Anti-D
 - IVIG
- Decrease antibody production
 - Rituximab
 - Steroids
 - Azathioprine and other immunosuppressants (eg, cyclophosphamide, cyclosporine, mycophenolate mofetil)
- Impair T and B cell interactions
 - Steroids
 - Rituximab
 - Other immunosuppressants
- Enhance platelet production
 - Thrombopoietic agents
 - Interleukin 11

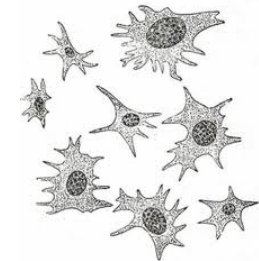
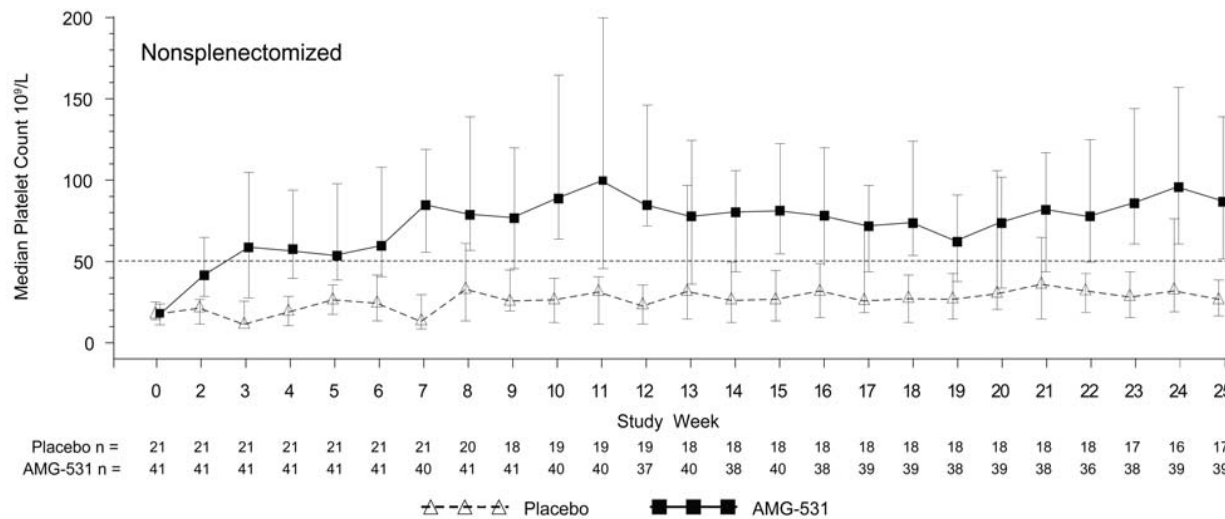
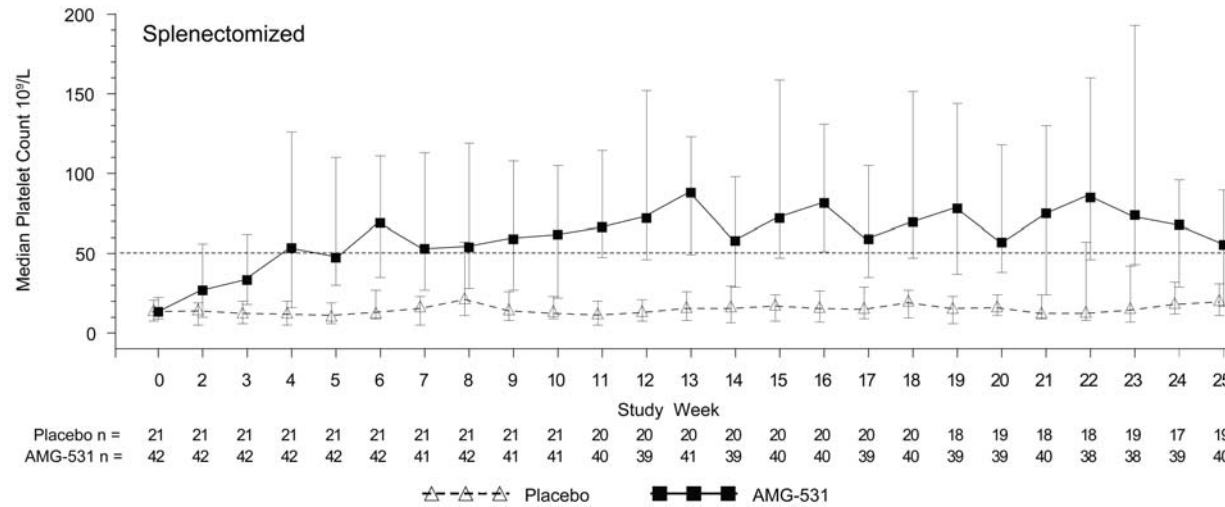


Thrombopoietin Levels in ITP

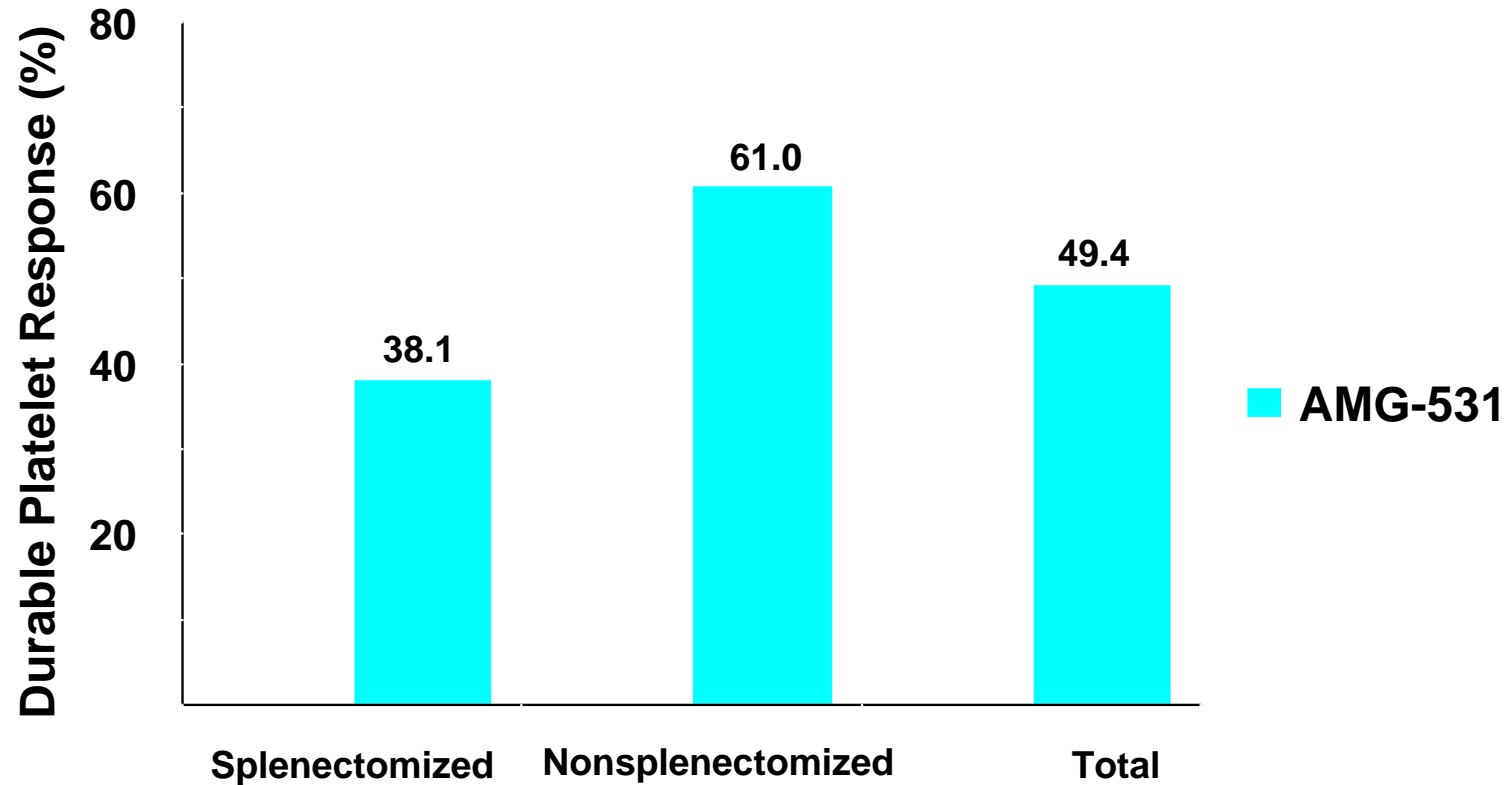


*Amegakaryocytic thrombocytopenia

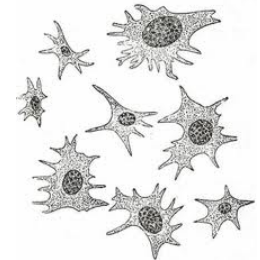
Romiplostim Trials – Platelet Count



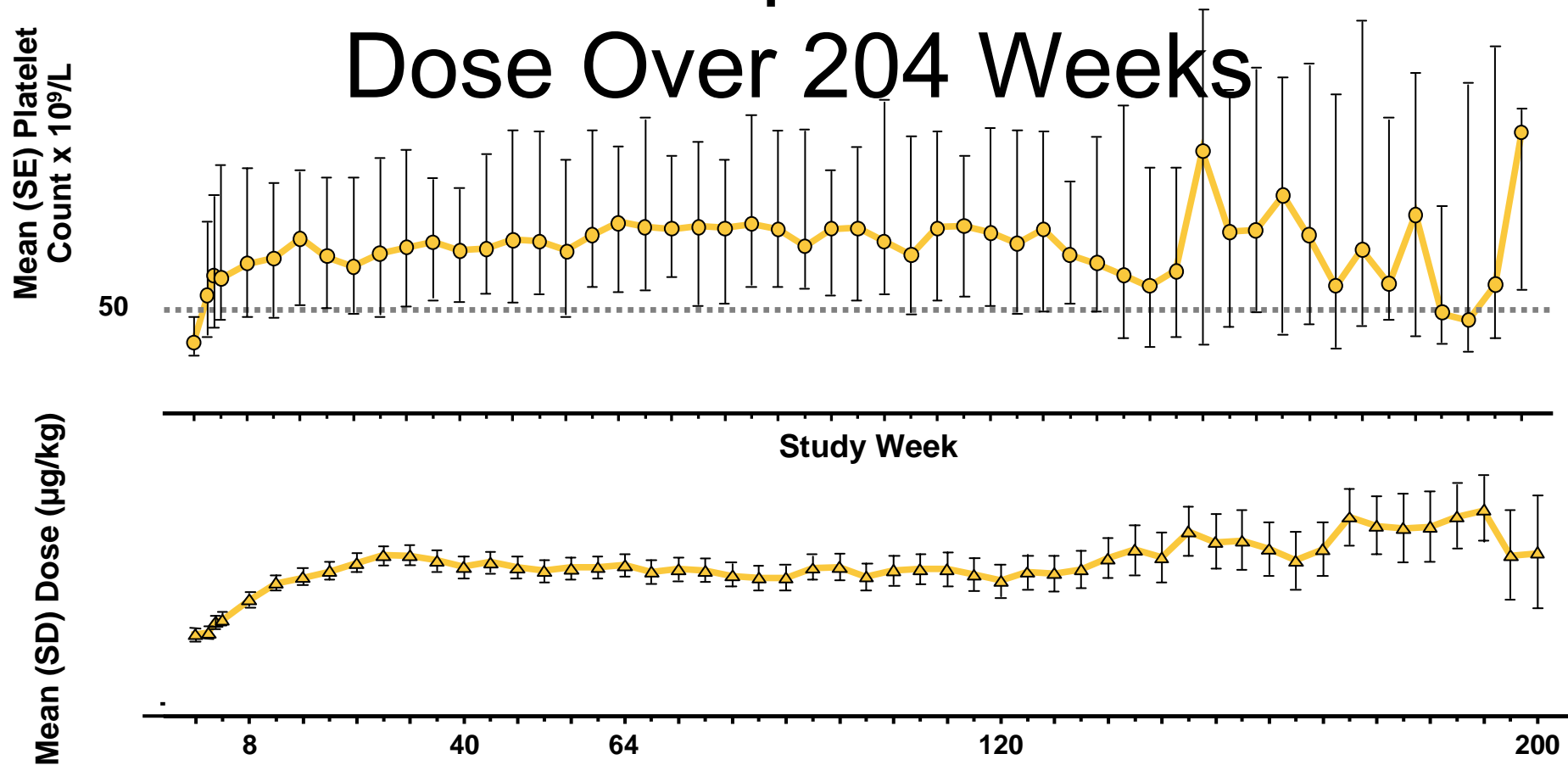
Durable Responses in Romiplostim Trials



Durable Response: Weekly platelet count $\geq 50,000$ on 6 of last 8 weeks of study; no rescue meds allowed



Mean Platelet Count and Romiplostim Dose Over 204 Weeks

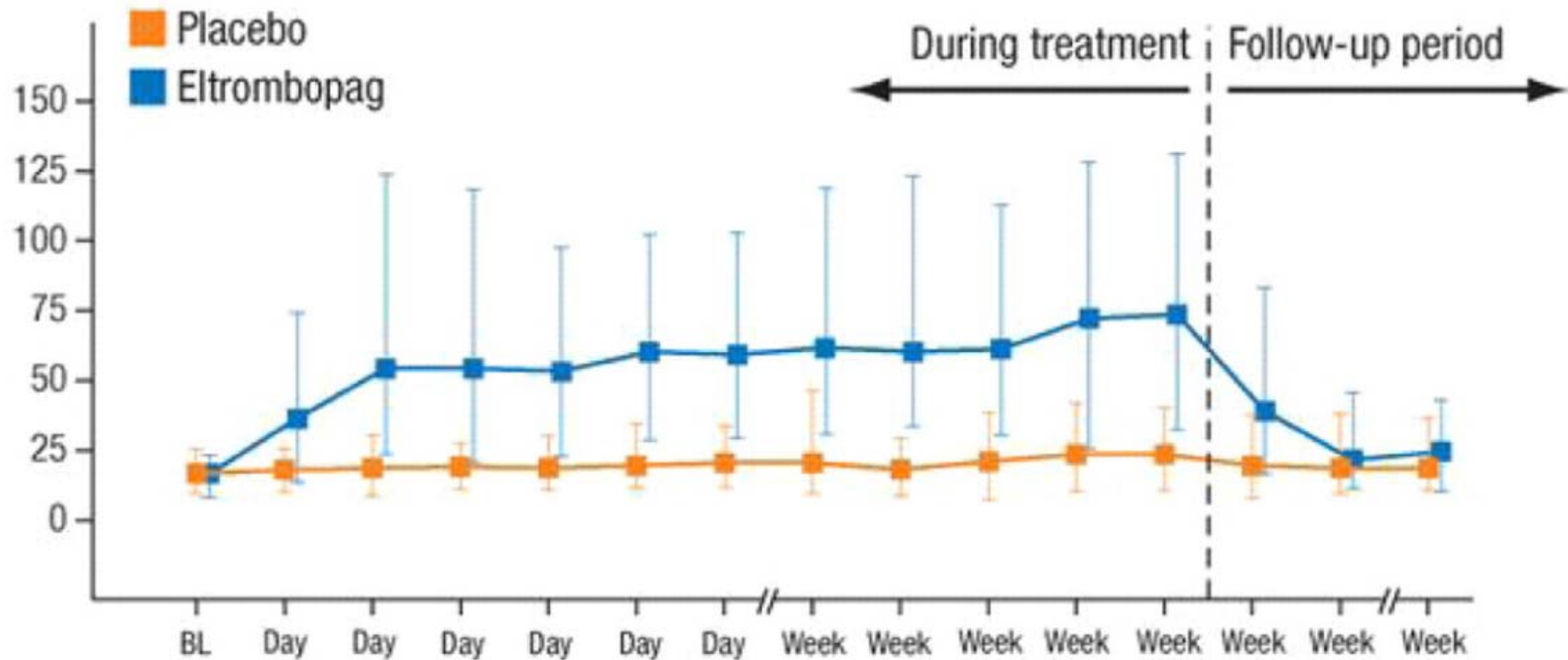


n is the number of patients with available platelet counts, excluding those who received rescue medications. Platelet counts within 8 weeks after receiving any rescue medications were excluded.

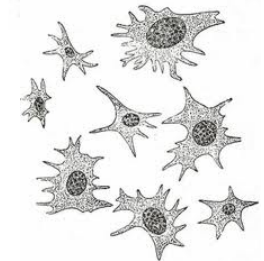
Kuter DJ, et al. *Blood*. 2008;112:Abstract 402.

Eltrombopag and Median Platelet Counts: RAISE

Median Platelet Count (x1,000/ μ L)

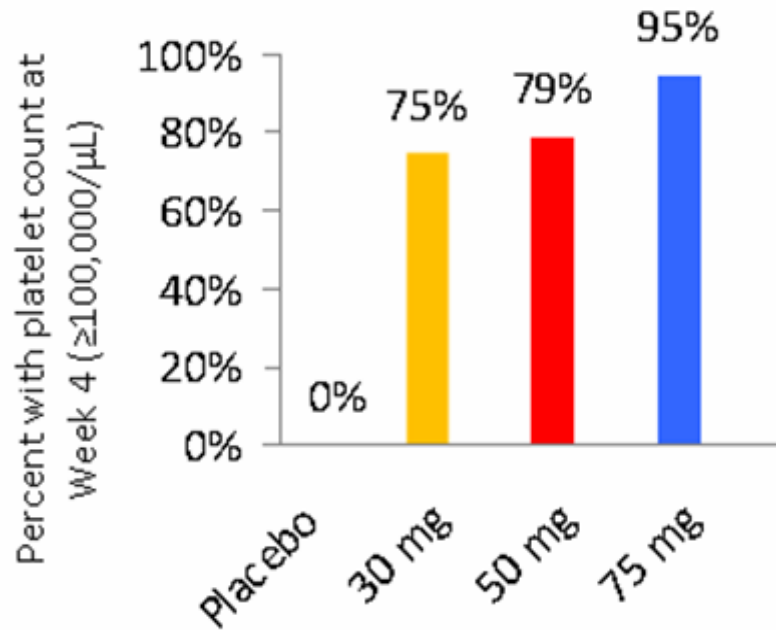


- Phase III clinical trial
- 26 weeks plus observation



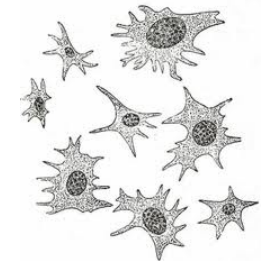
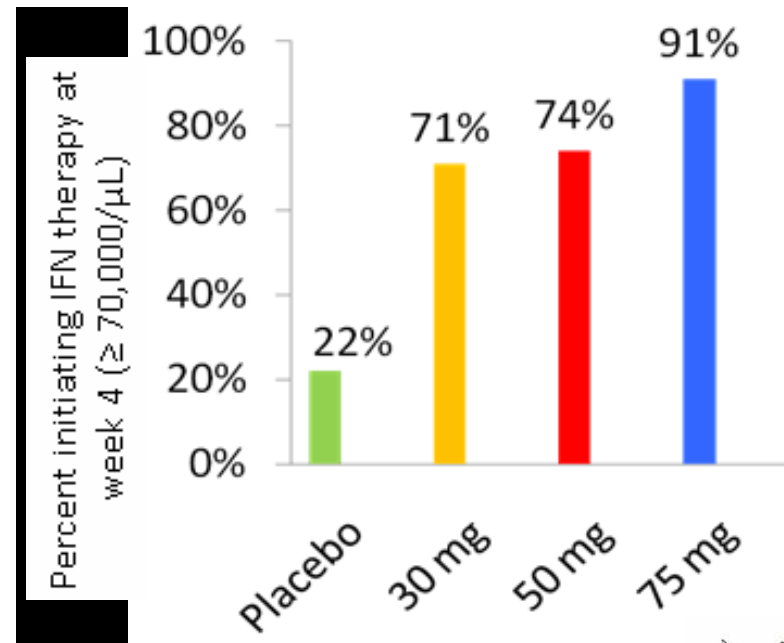
Eltrombopag Enhances Platelet Count and Ability to Initiate Interferon Therapy

Patients With $\geq 100,000$ Platelets / μL at 4 Weeks



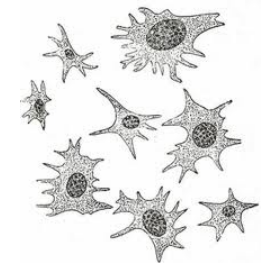
$P \leq 0.001$ for each group vs Pbo

Patients Entering Antiviral Phase

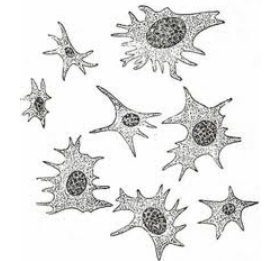
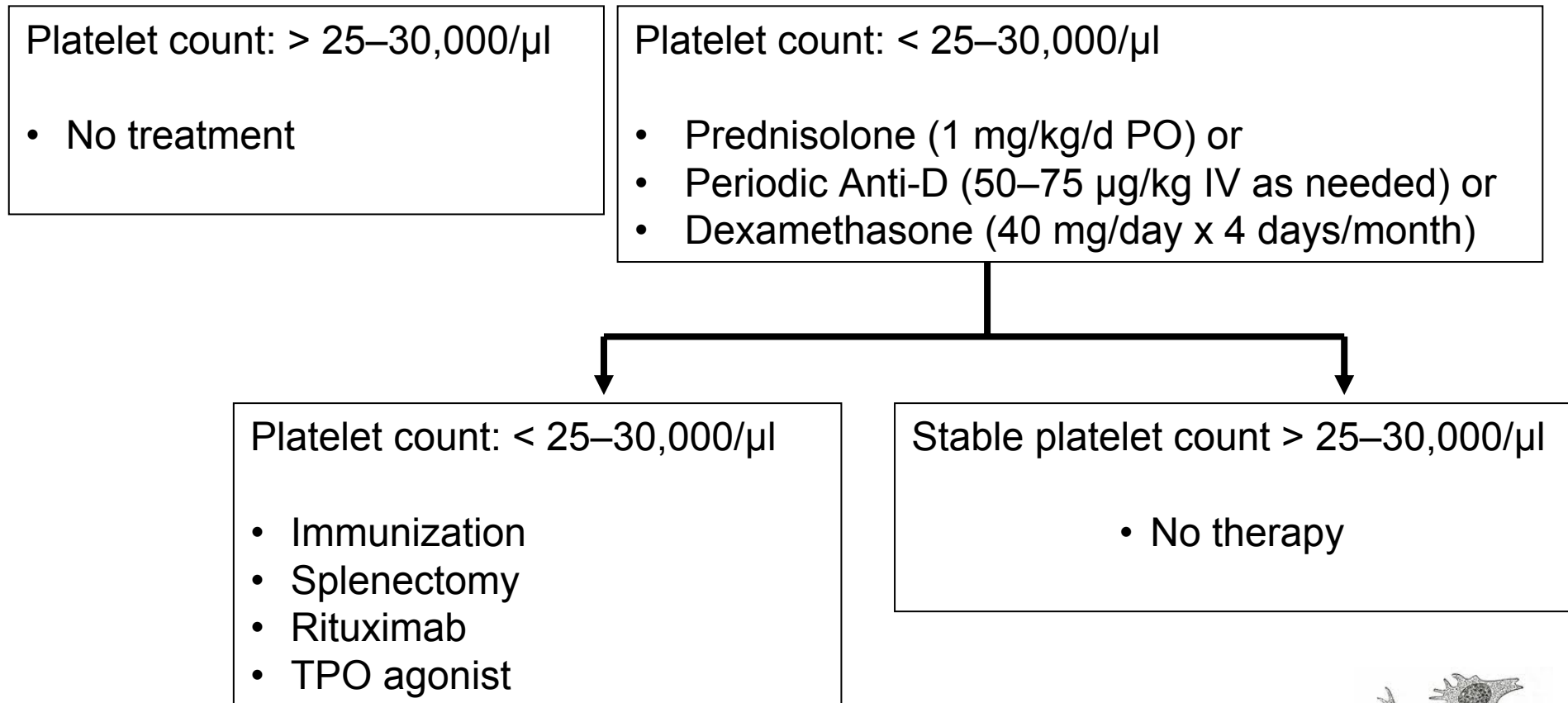


Emergency Treatment of Adult ITP

- IVIG (1.0 g/kg/d for 2–3 days) and/or
- Methylprednisolone (1.0 g/d x 3d)
- \pm Platelet transfusion
- \pm Factor VIIa



Initial Treatment of Adult ITP



Treatment of Patients Failing Splenectomy

Platelet count: < 25–30,000/ μ l



First-line Therapy

- Rituximab
- TPO agonist
- Prednisone
- Danazol/pred



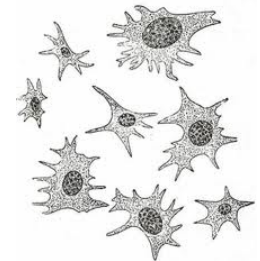
Second-line Therapy

- Azathioprine
- Oral cyclophosphamide
- Mycophenolate mofetil
- Cyclosporine



Third-line Therapy

- High-dose cyclophosphamide
- Combination chemotherapy
- Stem-cell transplantation



Wrapping it up...

- ITP is often a chronic disease in adults
- Multiple therapies may be needed over time
- Goal = prevention of complications
- Therapy needs to be tailored to the individual patient

