Chapter 3: Immune Thrombocytopenia: The Challenges of Achieving an Enduring Remission

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Immune thrombocytopenia (ITP)

- An autoimmune disorder that can be primary or secondary
- Primary ITP:
  - Isolated thrombocytopenia: platelet count < 100 × 10^9/L
  - Absence of other causes or disorders that may be associated with thrombocytopenia
  - Remains diagnosis of exclusion
  - Increased risk of bleeding
    - Bleeding is very heterogeneous

Rodeghiero F, et al. *Blood.* 2009;113(11):2386-2393.

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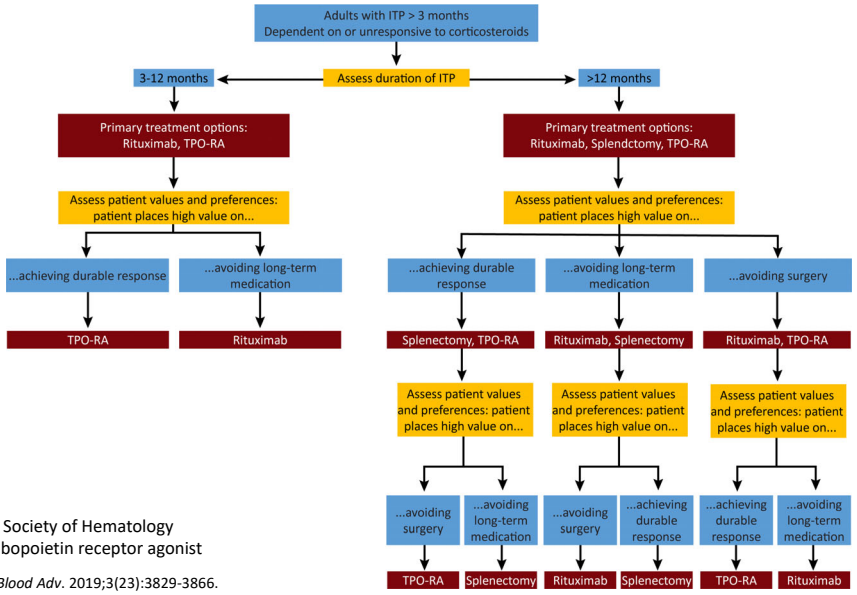
ASH 2019 guidelines for selection of second-line therapy in patients with ITP



ASH: American Society of Hematology
TPO-RA: thrombopoietin receptor agonist

Neunert C, et al. *Blood Adv.* 2019;3(23):3829-3866.

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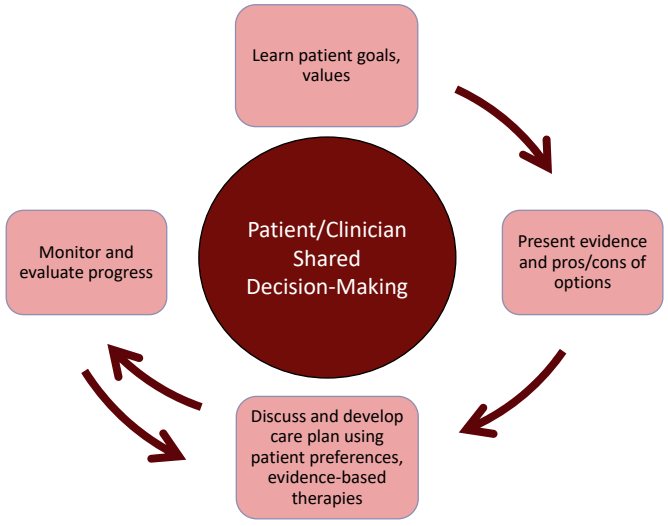
Shared decision-making



Adapted from Jackson WC. *J Fam Pract.* 2021;70(1 suppl [iii]):S4-S10.

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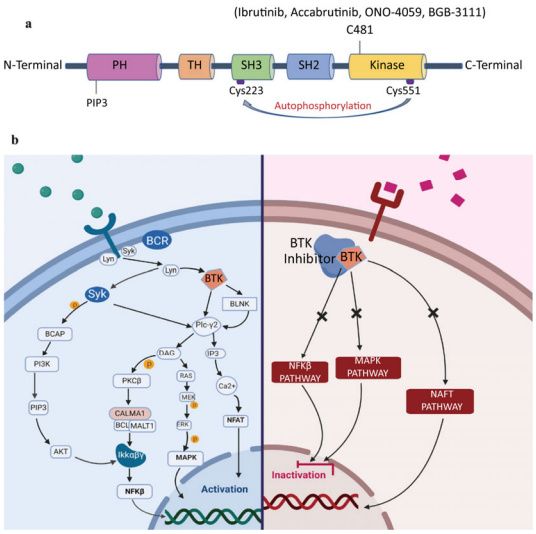
Emerging ITP therapies: Bruton's tyrosine kinase (BTK) inhibition

(a) Structure of BTK and (b) how BTK inhibitors work



- Blocks Fcγ-mediated macrophage destruction of platelets
- Blocks signaling through Fcγ in B cells
- Rilzabrutinib engineered to have less mitogen-activated protein kinase (MAPK) inhibition than other BTK inhibitors and therefore less effect on platelet function

Adapted from Xue C, et al. *Cancer Cell Int*. 2020 Sep 29;20:467, under CC attribution license 4.0.

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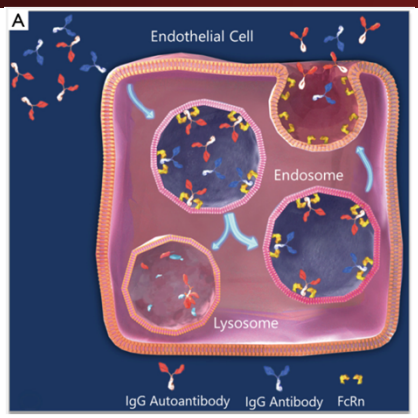
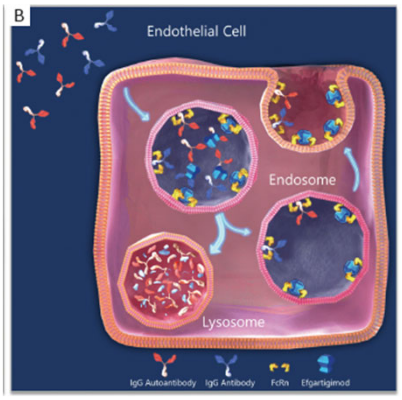
Emerging ITP therapies: FcRn blockade





(A) Under normal conditions, the neonatal Fc receptor (FcRn) protects IgG from degradation

- Inside the cell, FcRn binds IgG
- Unbound IgG enters the lysosome, where it is degraded
- IgG bound to FcRn is instead released from the cell via exocytosis
- Released IgG exacerbates ITP symptoms

(B) FcRn inhibitors may ameliorate ITP symptoms by disrupting the IgG recycling process

- FcRn inhibitors (eg, efgartigimod) bind to FcRn
- Ingested IgG is now unable to bind to FcRn
- Unbound IgG enters the lysosome and is degraded
- Degraded IgG is not available to cause ITP symptoms

Patel DD, Bussel JB. *J Allergy Clin Immunol.* 2020;146(3):467-478. Images reprinted from Newland AC, McDonald V. *Ann Blood*. 2021;6:6, under a CC BY-NC-ND 4.0. license.

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