Novel Therapeutics in Pediatric Hematology

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Learning Objectives

- Review the recent clinical trials data on DOAC use in pediatrics
- Compare novel treatments for hemophilia including extended half-life factor, factor mimetics, rebalancing agents, and gene therapy
- Discuss the risks and benefits of gene therapy for hemoglobinopathies including thalassemia and sickle cell disease

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Disclosures

- I have no financial disclosures
- I will not be recommending off-label use of medicines, but will mention several

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Outline

- Immune Thrombocytopenic Purpura (ITP)
  - Thrombopoietin agonists
- Thrombosis
  - Direct Oral Anticoagulants (DOACs)
- Hemophilia
  - Extended half-life factor
  - Factor mimetics
  - Rebalancing agents
  - Gene therapy
- Hemoglobinopathies
  - Gene therapy

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Immune Thrombocytopenic Purpura (ITP)

- Immune trigger
- Autoimmune destruction of platelets
- Petechiae, bruising, purpura
- Diagnosis of exclusion
  - Isolated thrombocytopenia
  - Absence of constitutional symptoms
- Self-limited in children

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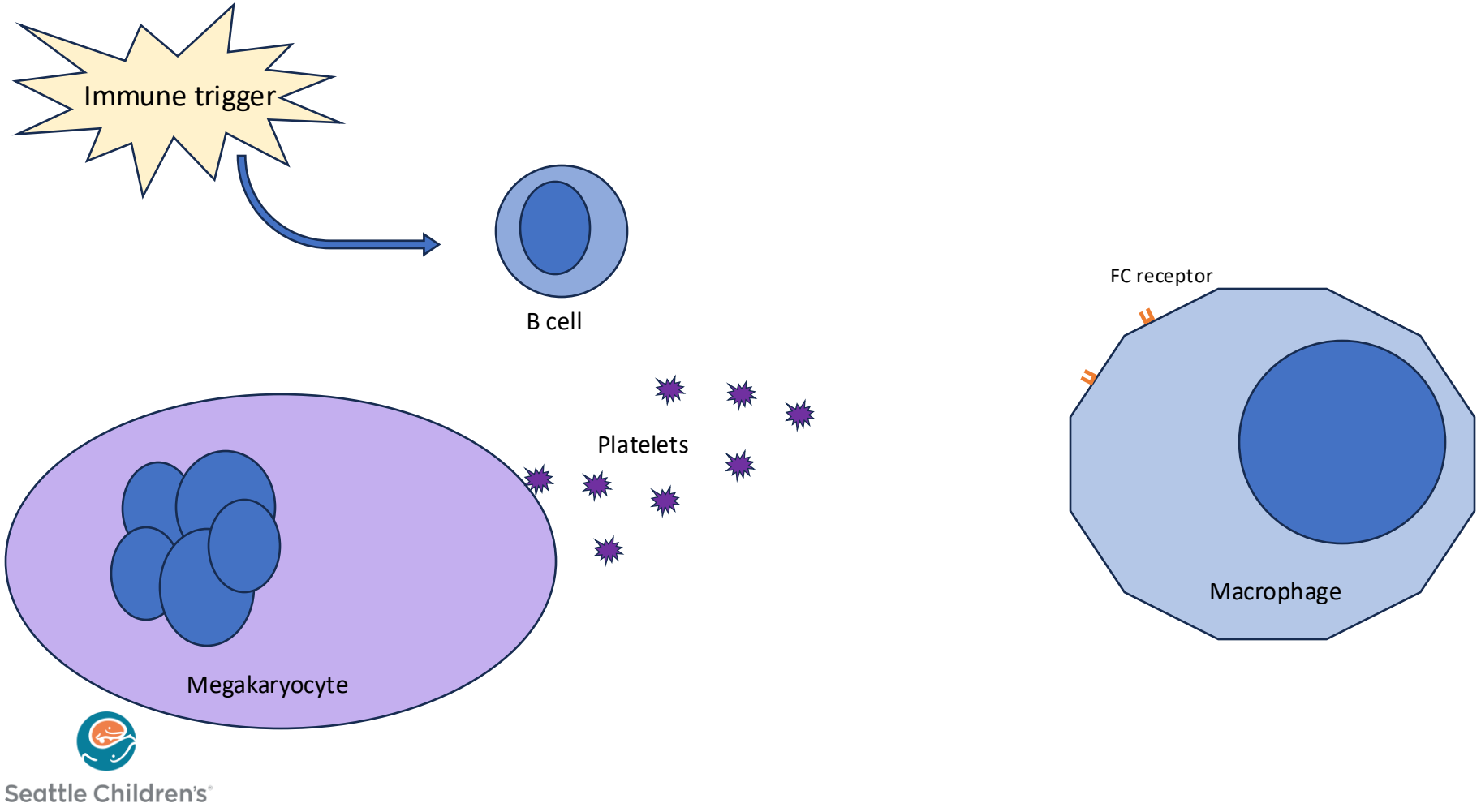

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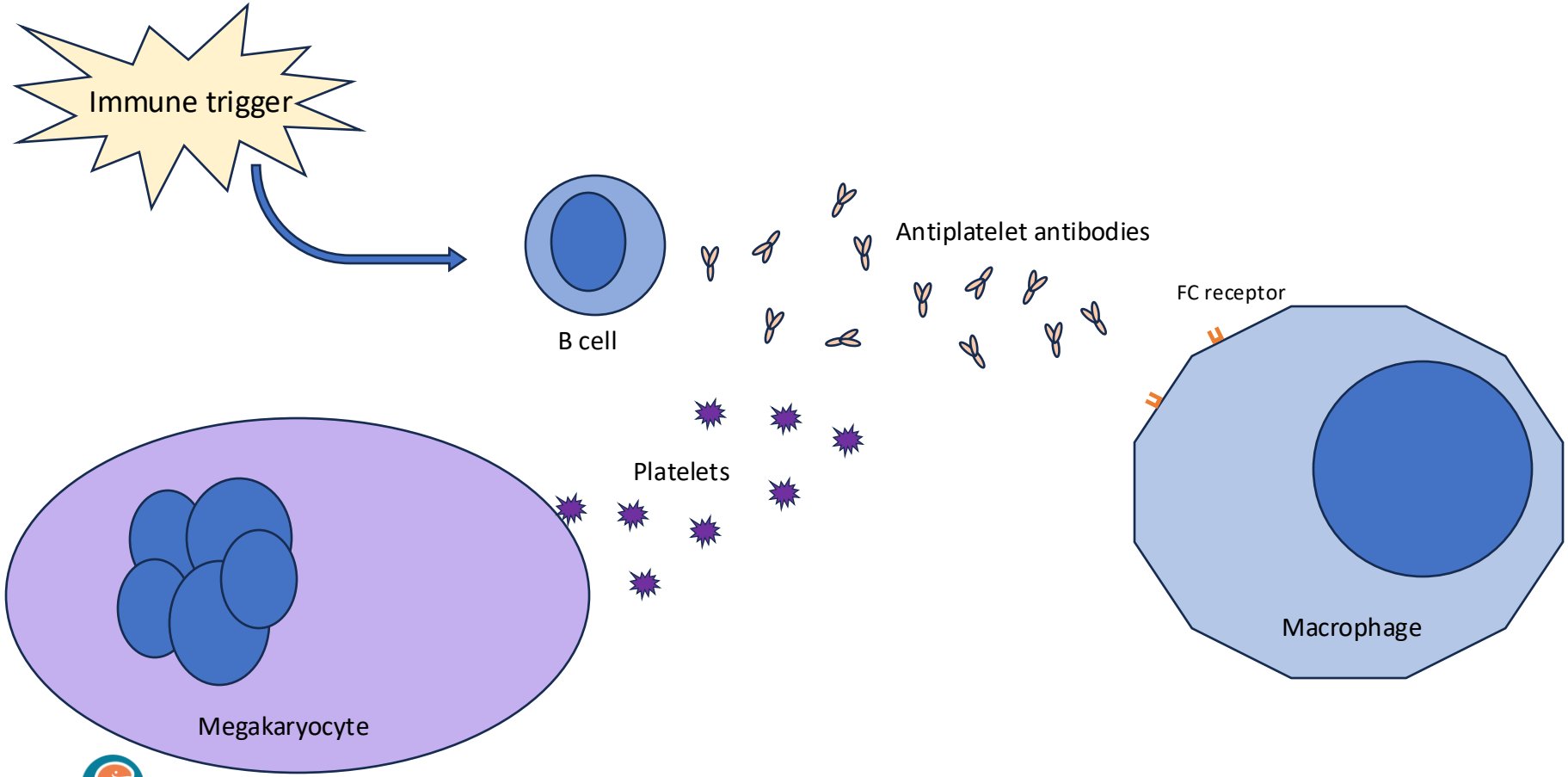

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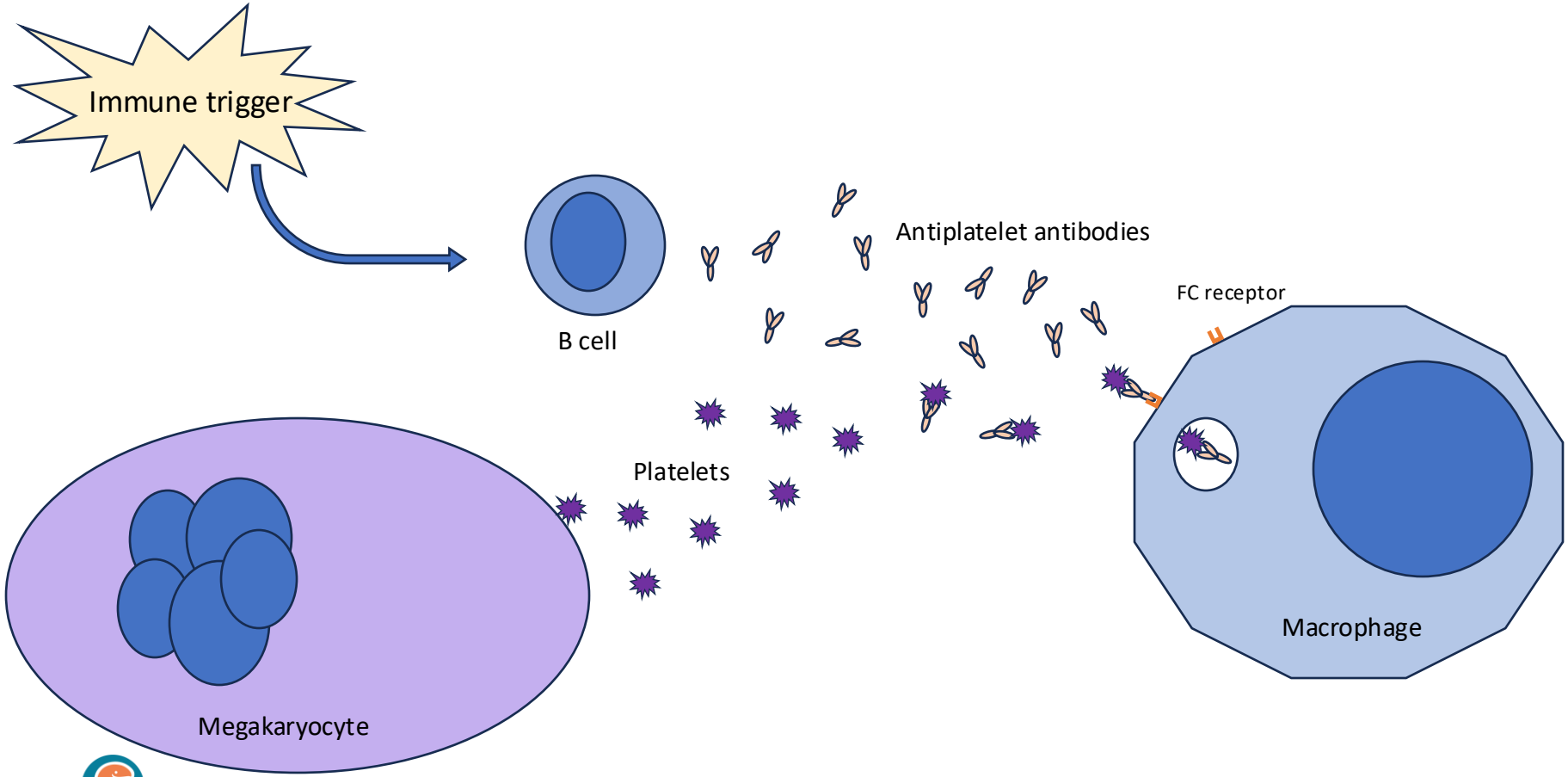

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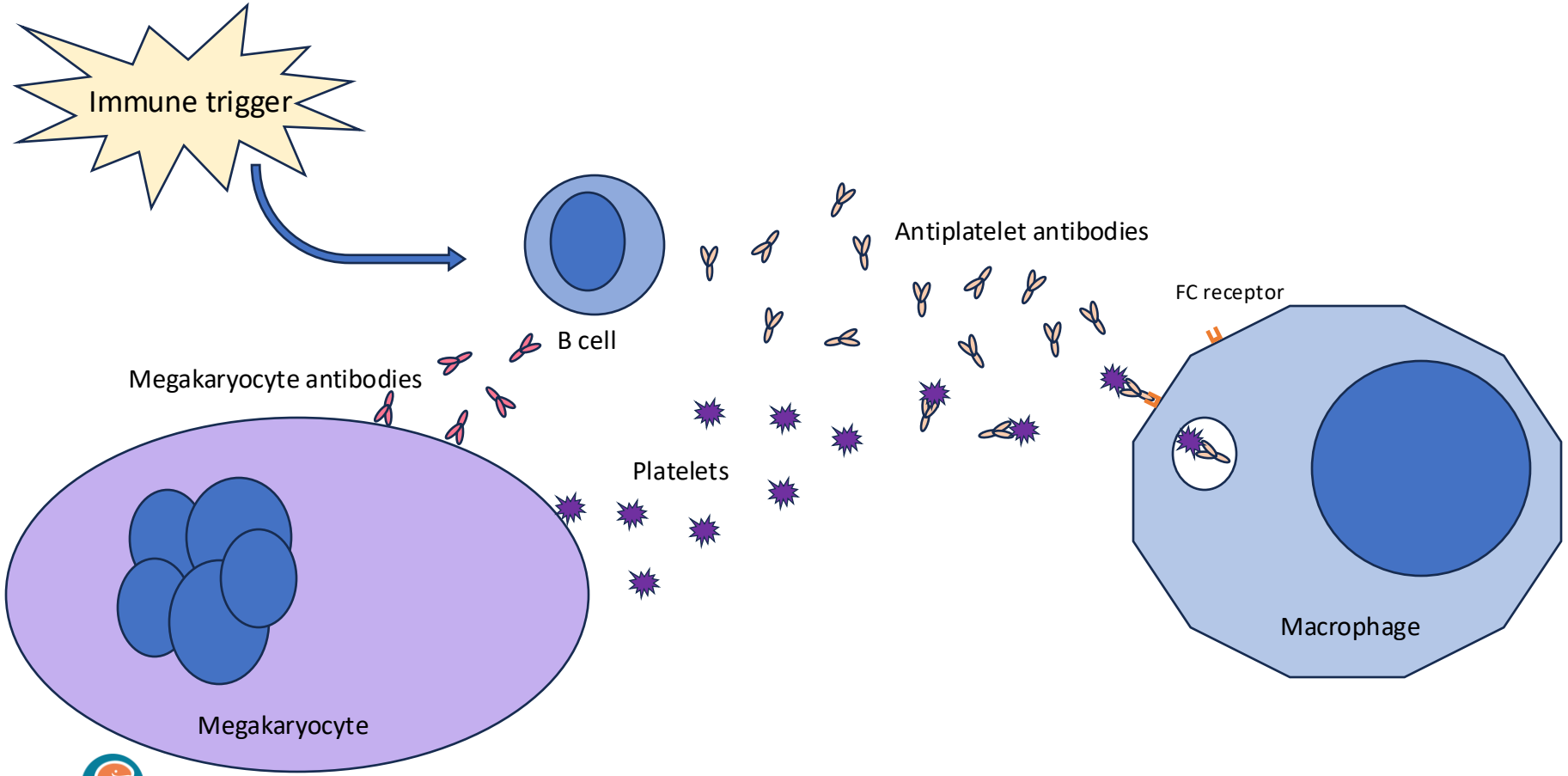

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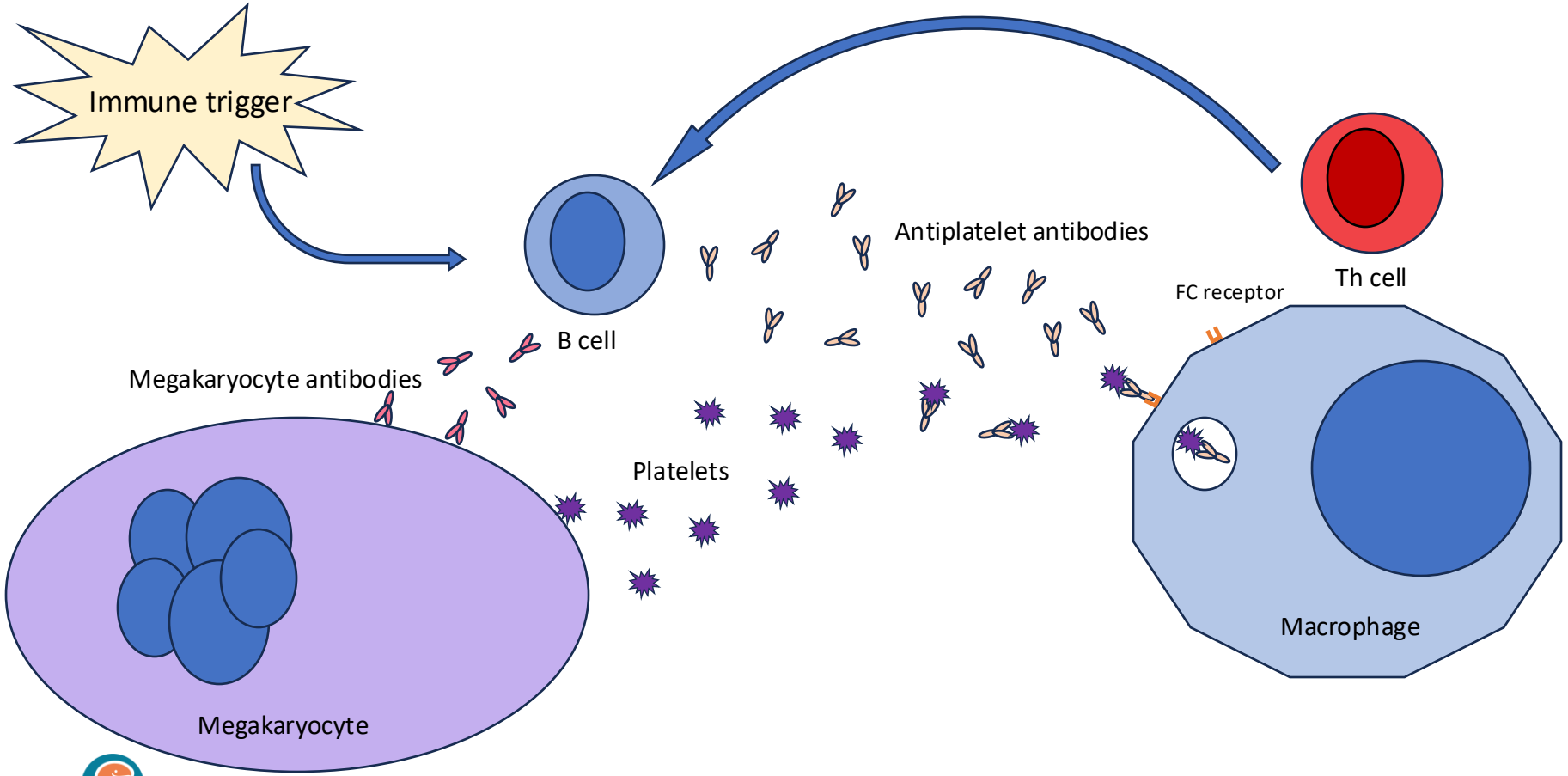

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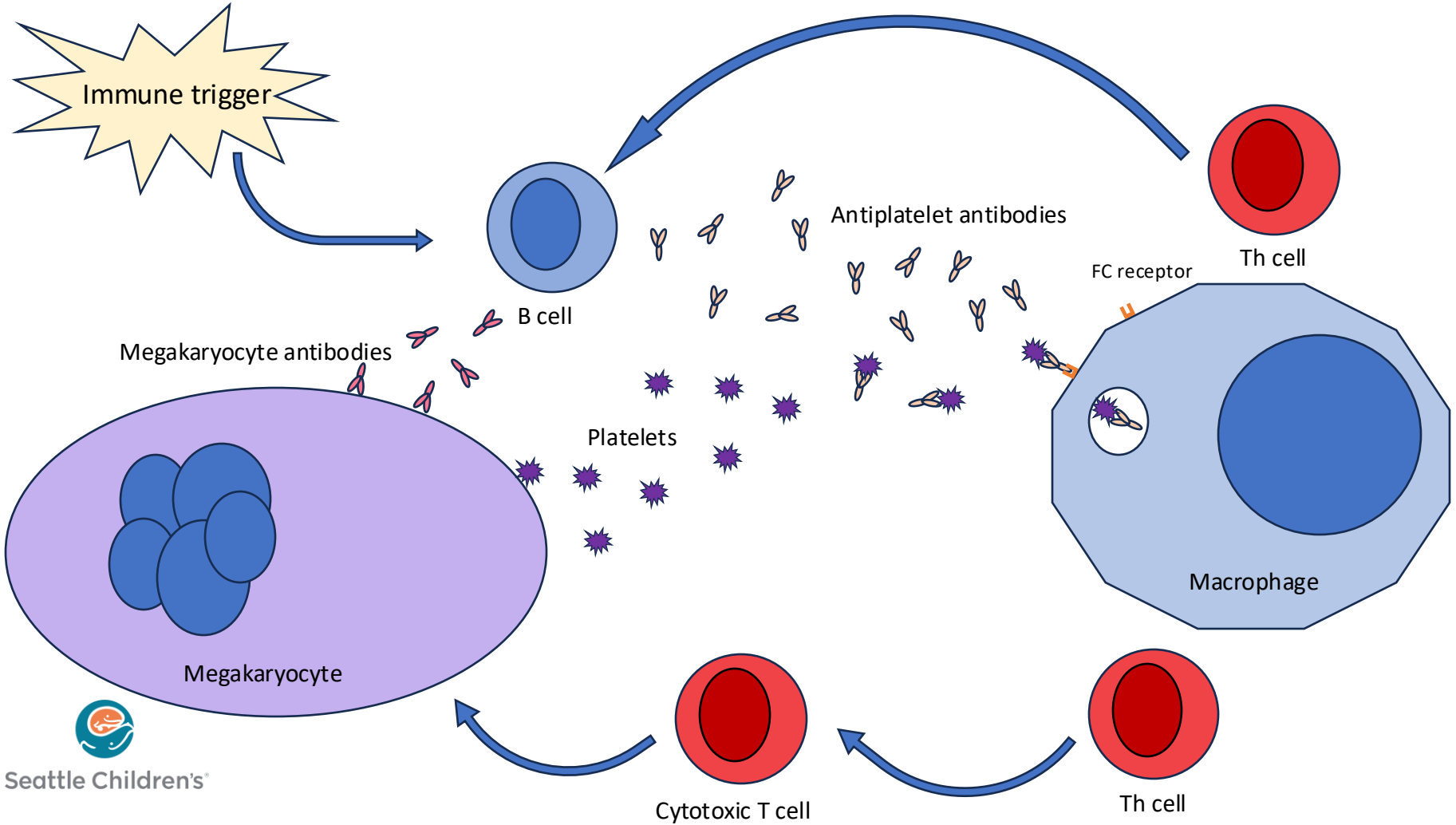

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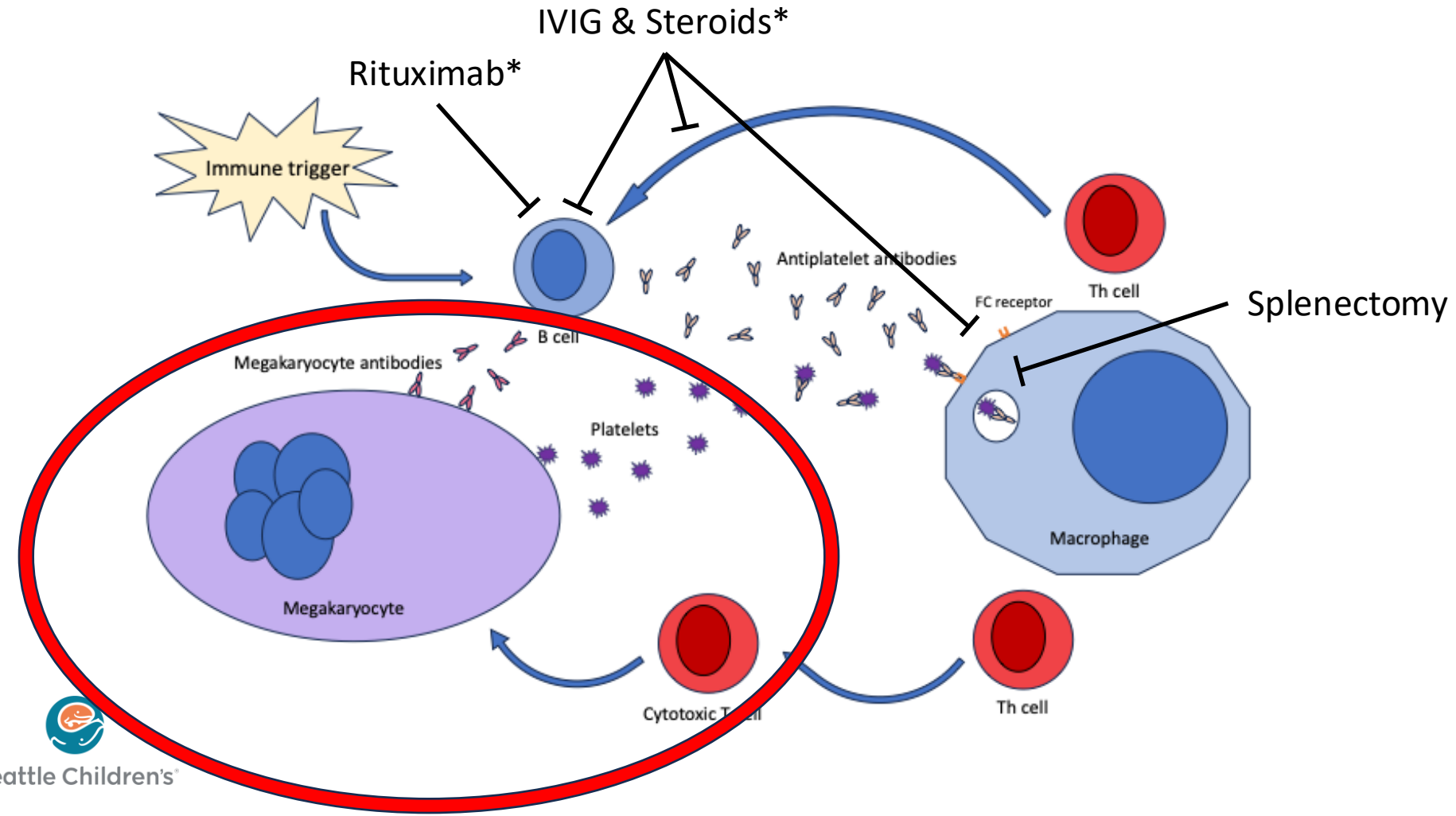

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Thrombopoietin Receptor Agonists (TPO-RAs)

- A class of medications that stimulates platelet production by mimicking the action of thrombopoietin (TPO)
- Each drug interacts with the TPO receptor on the surface of megakaryocytes
- Increase megakaryocyte proliferation, increase platelet production
- Eltrombopag (2015), Romiplostim (2018), Avatrombopag (2025)

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Eltrombopag (Promacta)

- Targets the transmembrane domain of TPO-R
- Chronic ITP in children ≥ 1 year old
- Orally administered once daily (tablets, powder for suspension)
- Response seen in 1-2 weeks
- Must not be taken within 4 hours of any food or medication with polyvalent cations (Ca, Mg)
- Titrate to keep platelet count 50-200 x 10^9/L

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Romiplostim (Nplate)

- Targets the extracellular domain of TPO-R
- Chronic ITP in children ≥ 1 year old
- Subcutaneously administered once weekly (at infusion clinic)
- Response seen in 4-9 days
- No food interactions
- Titrate to keep platelet count 50-200 x 10^9/L

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Avatrombopag (Doptelet)

- Targets the transmembrane domain of TPO-R
- Chronic ITP in children ≥ 1 year old
- Orally administered once daily (tablets, capsule with granules)
- Response seen in 3-5 days
- No food interactions
- Titrate to keep platelet count 50-200 x 10^9/L

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FULL TEXT ARTICLE

Avatrombopag for the treatment of children and adolescents with immune thrombocytopenia (AVA-PED-301): a multicentre, randomised, double-blind, placebo-controlled, phase 3b study

Rachael F Grace MD, Göksel Leblebisatan Prof, Yesim Aydinok Prof, Şule Ünal Prof, John D Grainger MD, Jessica Zhang MS, Linda Smallwood MS, Emily de León MS and Brian D Jamieson MD

Lancet Haematology, The, 2025-07-01, Volume 12, Issue 7, Pages e494-e504, Copyright © 2025 Elsevier Ltd

- 75 participants age 1-18
- Chronic ITP, not responsive to other treatments
- Randomized 3:1 to avatrombopag or placebo
- 12-week treatment period, open-label extension phase
- 28% of participants in the avatrombopag group had a durable response (PLT ≥ 50 for at least 6 of the final 8 weeks)
- Most common adverse events were HA, fever, cough, URI
- No thromboembolic events

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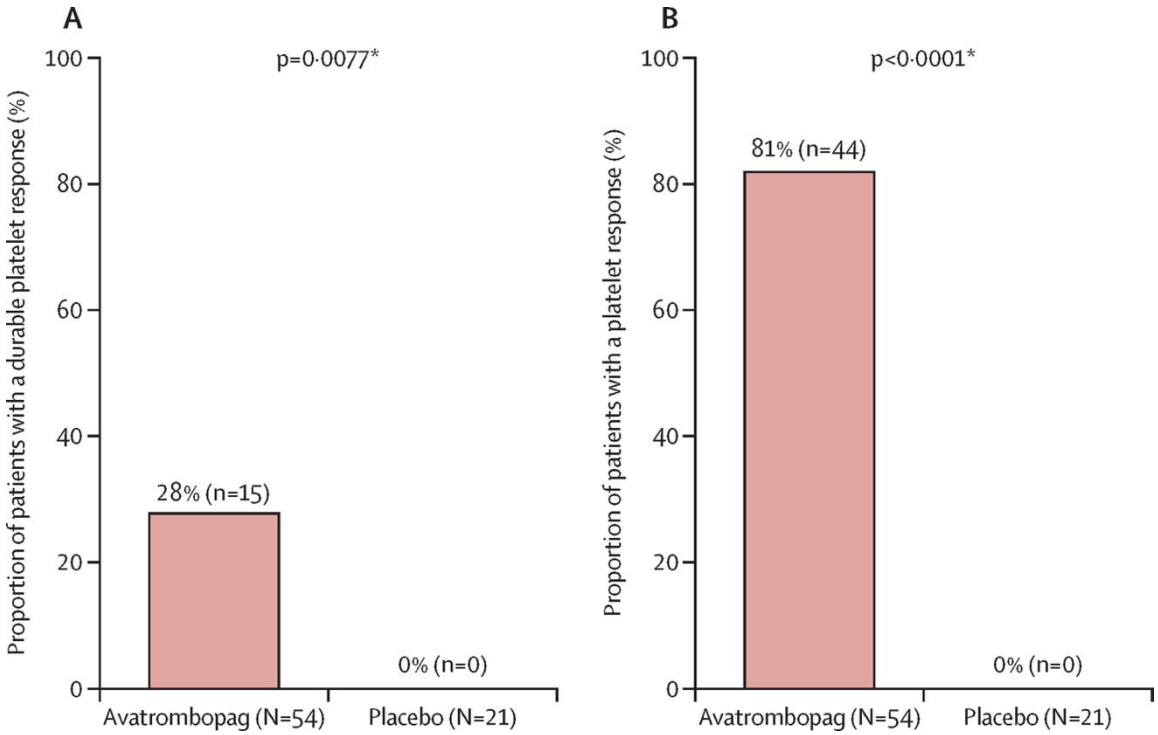

- B shows the alternative endpoint- at least two consecutive PLT counts ≥ 50 without any additional rescue therapy

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Immune Thrombocytopenic Purpura (ITP)

- Current State
  - Treatment of acute ITP remains observation, steroids, and IVIG
  - Treatment of chronic ITP is increasingly TPO-RAs
- Future State
  - Studies exploring up-front use of TPO-RAs
  - Other therapies being studied include Bruton tyrosine kinase (BTK) inhibitors, monoclonal antibodies that target BAFF-R, FcRn antagonists, plasma cell inhibitors, and more

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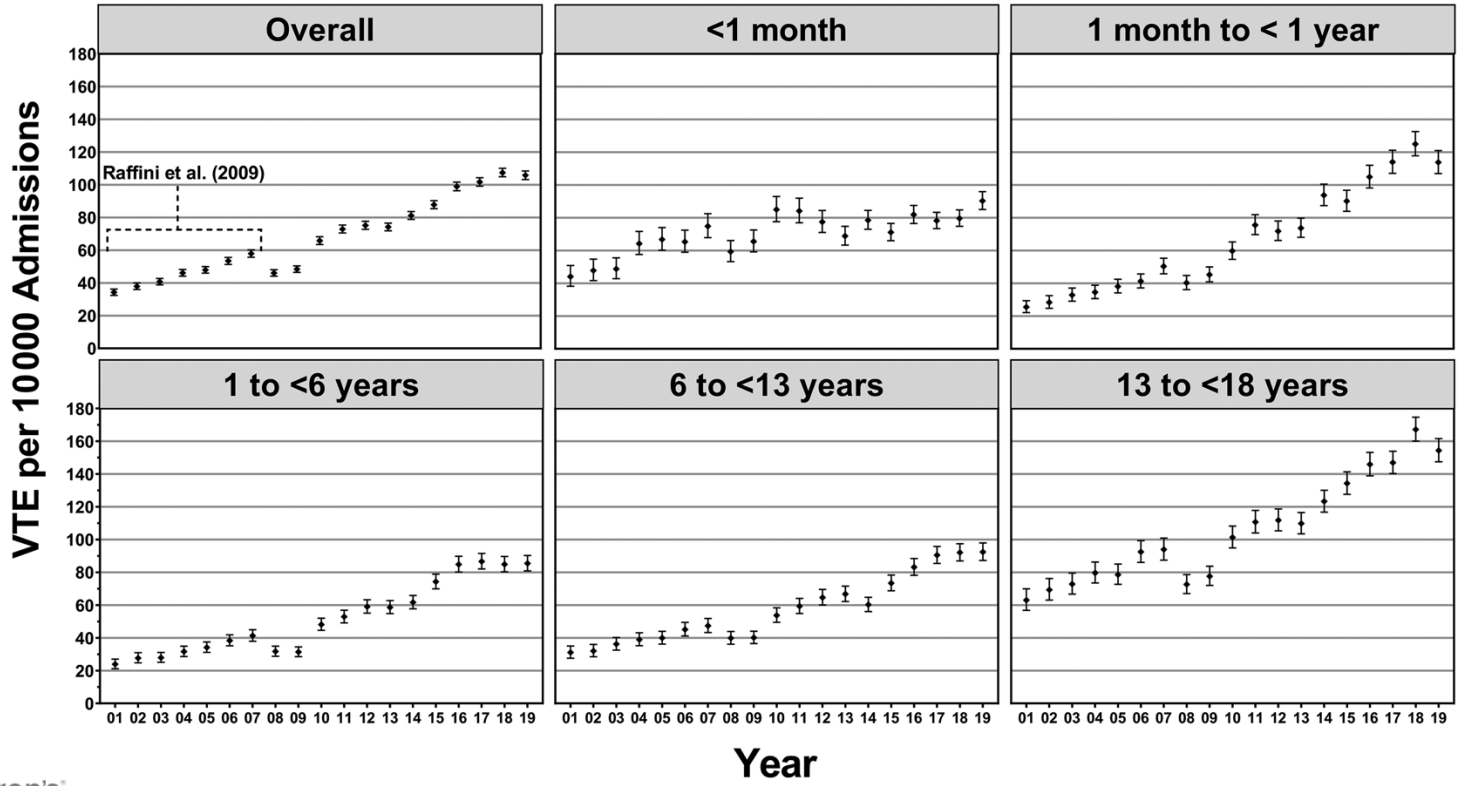
Thrombosis



Rates of VTE over time, from 2001-2019, Pediatric Health Information System

O'Brien et al. The Continued Rise of Venous Thromboembolism Across US Children's Hospitals. Pediatrics. 2022

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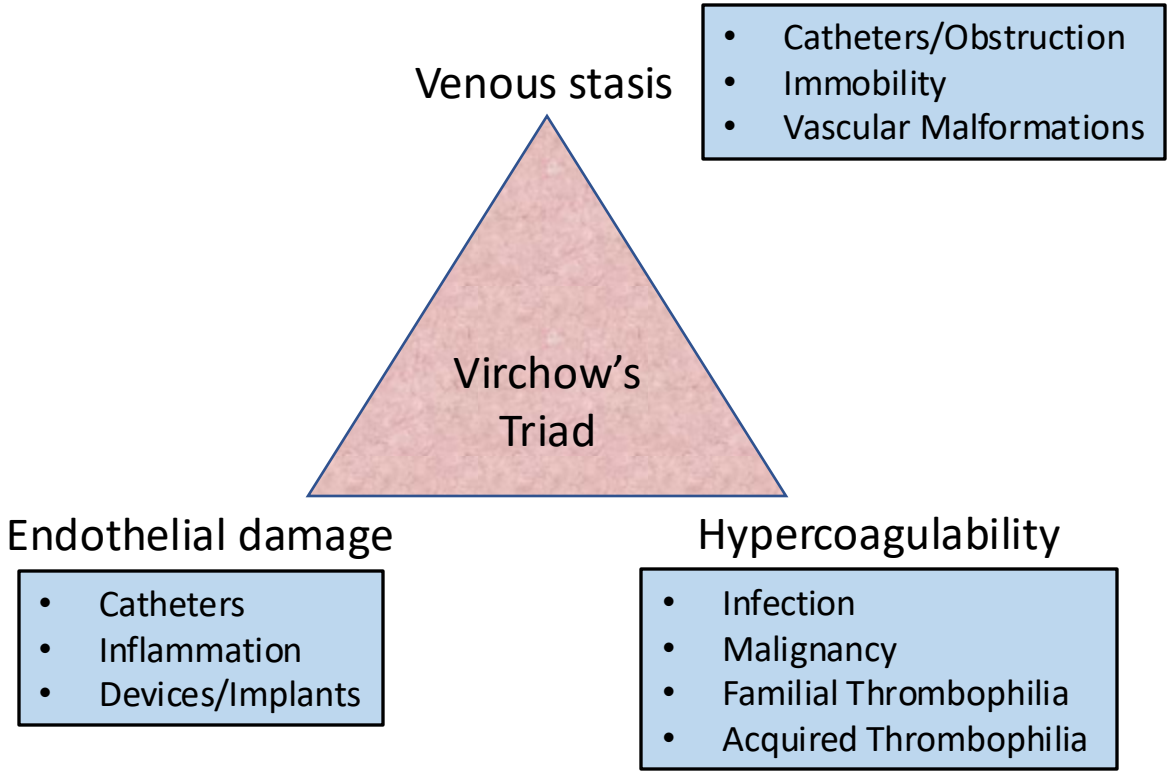
Thrombosis



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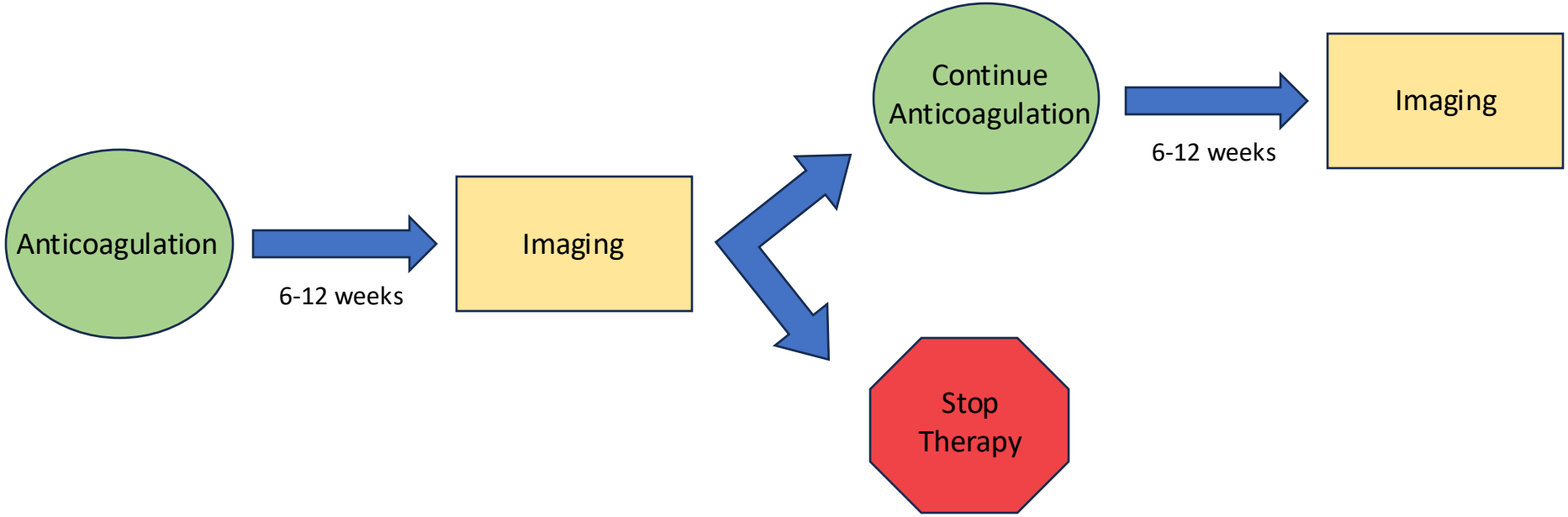
Anticoagulation

- Goals of Treatment
  - Resolution of thrombus
  - Prevention of recurrence
  - Prevention of post-thrombotic syndrome

- Secondary Goals of Treatment
  - Maintenance of quality of life
  - Prevention of bleeding

Anticoagulation



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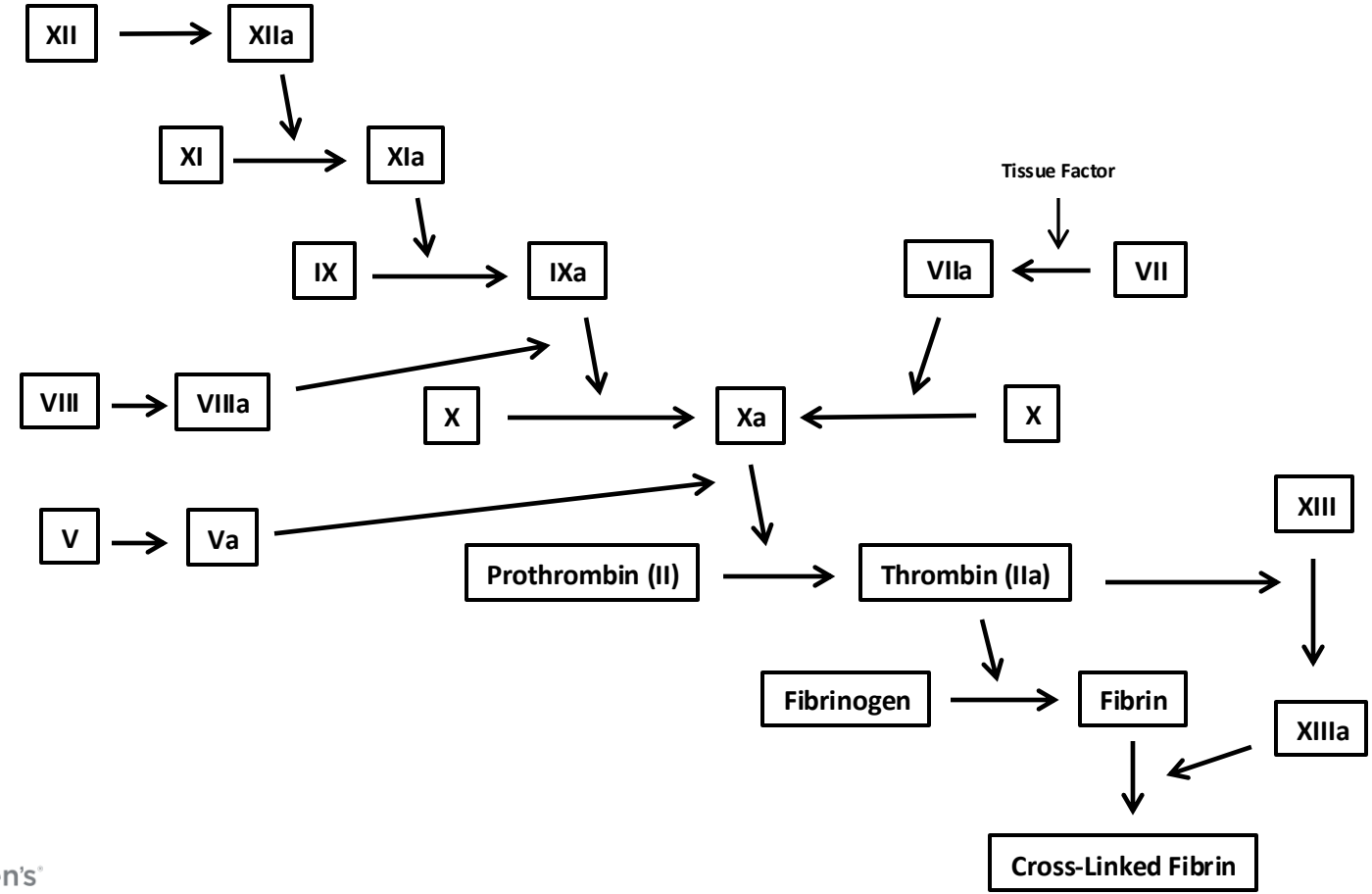

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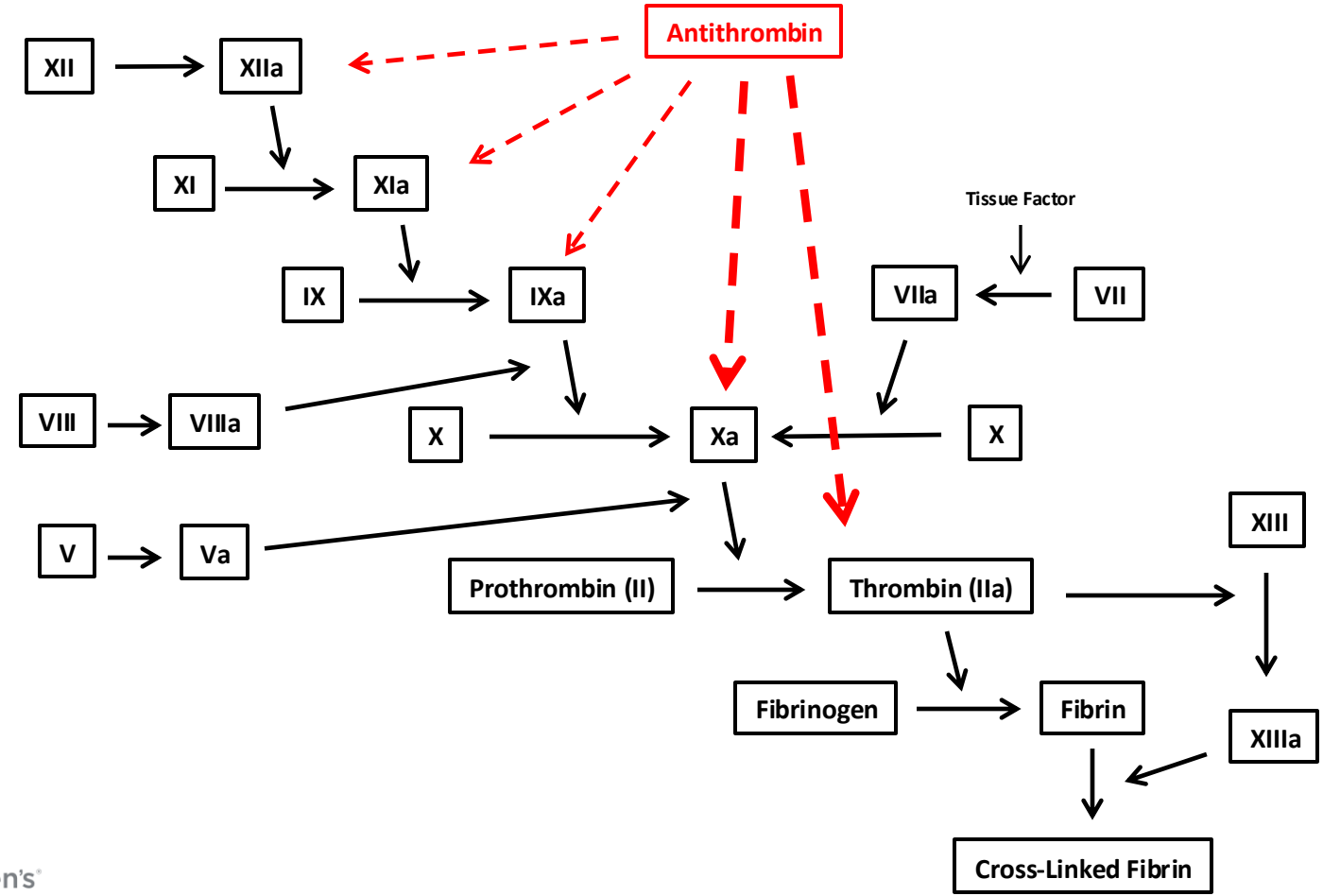

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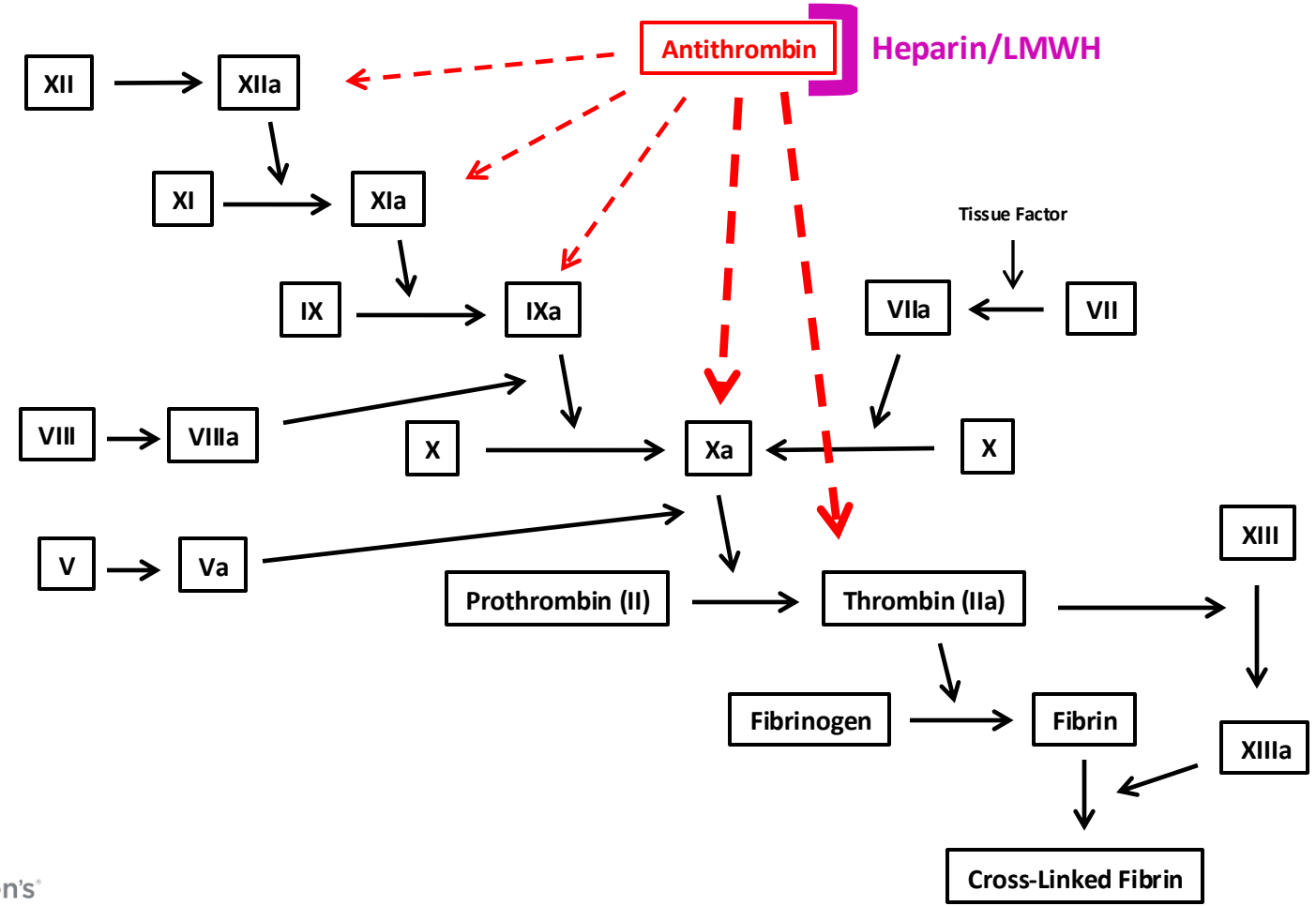

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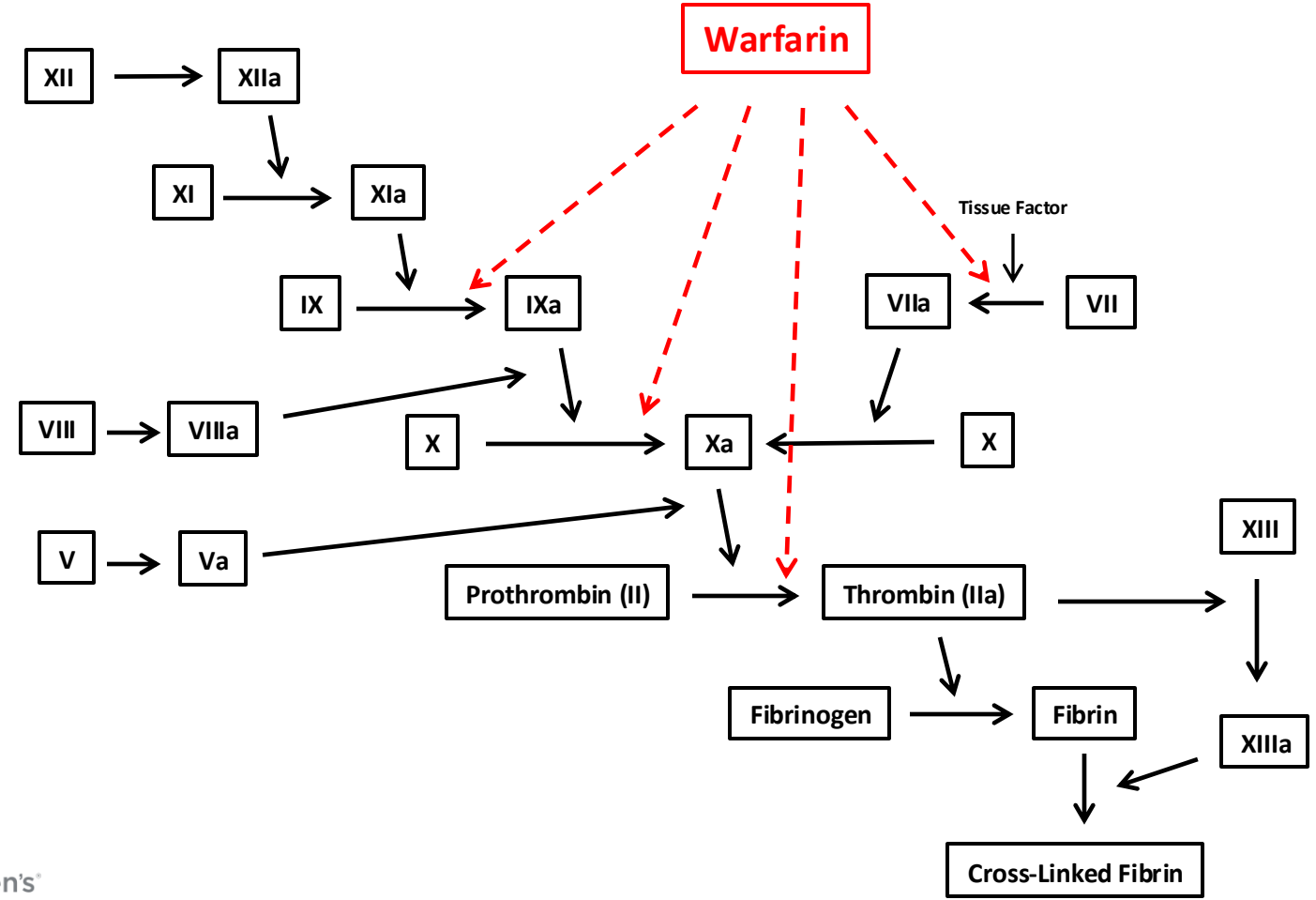

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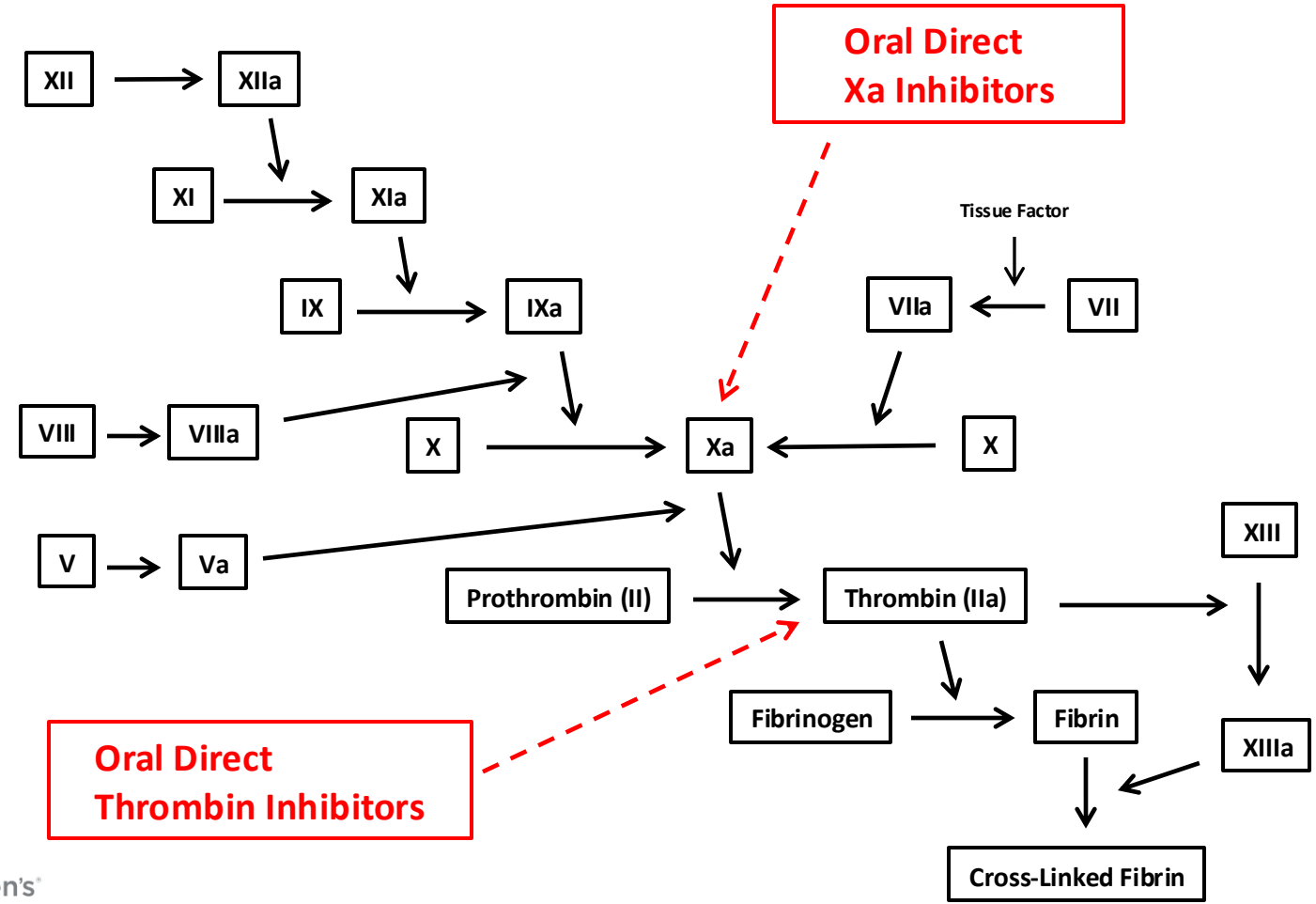

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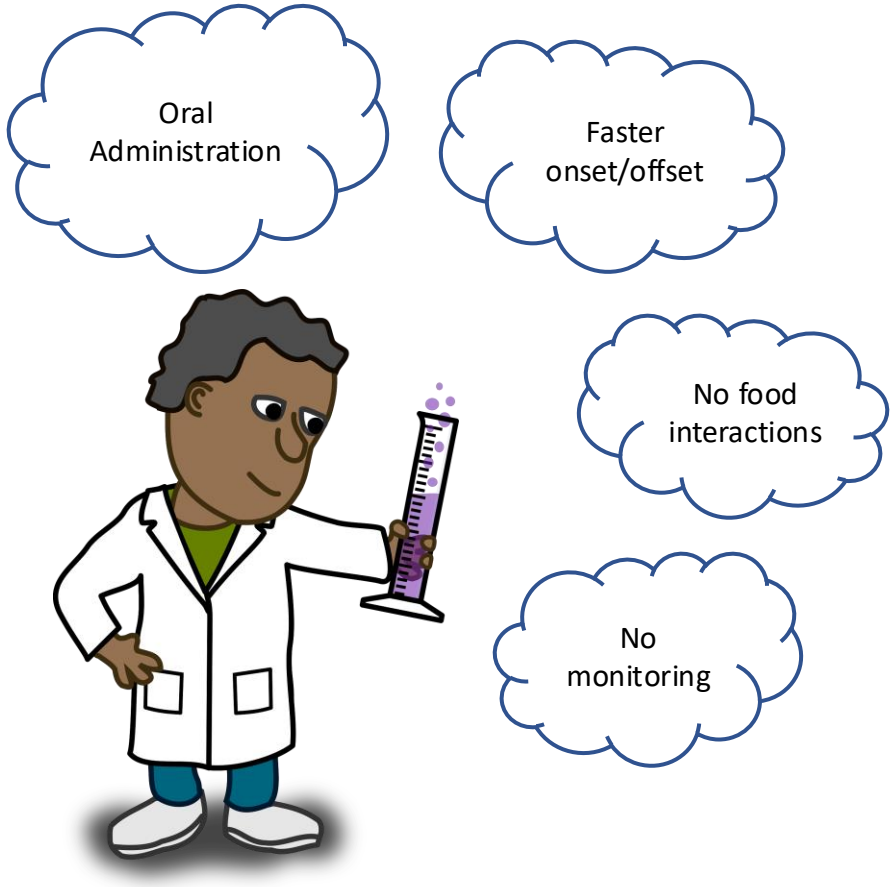
Direct Oral Anticoagulants (DOACs)

Designing the perfect anticoagulant



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Characteristic	Direct thrombin inhibitor	Direct FXa inhibitors			
	Dabigatran	Apixaban	Betrixaban	Edoxaban	Rivaroxaban
Oral bioavailability, %	3–7	52.3	34	62	66–100
Plasma protein binding, %	35	87	60	55	92–95
Renal excretion, %	80	27	17.8	50	50
Median T_{max}, h					
Single dose	1.25–1.5	1.5–1.8[a]/2.5–3.3[b]	3–4	1.0–1.5	0.5–0.6[a]/1.5–3[b]
Multiple dose	1.5			1.0–3.5	
Mean $t_{1/2}$, h					
Single dose	7–9	3.6–6.8[a]/11.1–26.8[b]	19–27	5.79–10.7	3.24–4.15[a]/7–17[b]
Multiple dose	14–17			8.75–10.4	
Interactions					
P-gp substrate					
Inducers	Decrease exposure	Decrease exposure	Decrease exposure	Not relevant	None
Inhibitors	Increase exposure	Increase exposure	Increase exposure	Increase exposure	Increase exposure
CYP3A4 substrate					
Inducers	None	Decrease exposure	None	None	Decrease exposure
Inhibitors	None	Increase exposure	None	None	Increase exposure

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Albisetti. Hamostaseologie. 2020 Feb;40(1):64-73.

Dabigatran

- DIVERSITY Trial:
  - A randomized, controlled, open-label, phase 2b/3, non-inferiority trial of dabigatran vs. standard of care for treatment of VTE in children
  - 234 children were initially treated with SOC (UFH or LMWH) and then randomized (2:1) to receive oral dabigatran twice daily for 3 months
  - The follow-up study kept subjects on Dabigatran for up to 12 additional months for prevention of recurrent VTE

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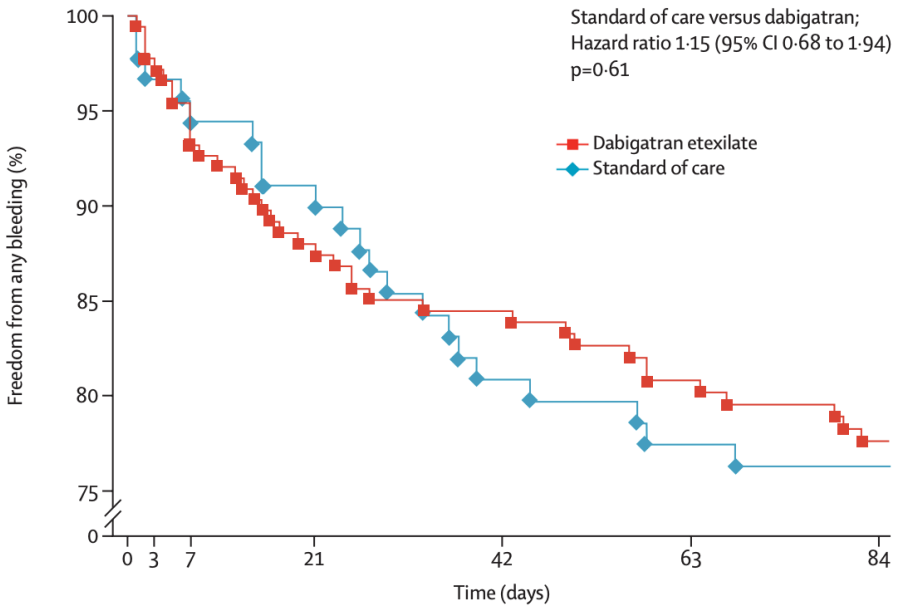
Dabigatran

	Standard-of care-group (n=90)	Dabigatran group (n=177)
Primary efficacy endpoint and its individual components (randomis		
Composite primary endpoint (complete thrombus resolution, freedom from recurrent venous thromboembolism, and freedom from venous thromboembolism-related death) met	38 (42%)	81 (46%)
Complete thrombus resolution	38 (42%)	81 (46%)
Freedom from recurrent venous thromboembolism	83 (92%)	170 (96%)
Freedom from venous thromboembolism-related death	89 (99%)	177 (100%)



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Halton et al. Lancet Haematol. 2021 Jan;8(1):e22-e33

Dabigatran

ADULT DATA	PEDIATRIC DATA	FDA PED APPROVAL
Adult Approval since 2010 Afib, VTE tx, VTE ppx	**DIVERSITY Trial published 2021** Non-inferiority to SOC for tx of VTE and for prevention of recurrent VTE	Approved in June 2021 for children >3 months

DOSAGE FORMS

Notes

- ++ GI toxicity (dyspepsia, GERD, abdominal pain)
- Rare use in adults
- Oral pellets only available from one specialty pharmacy
- Idarucizumab for reversal (no peds data)

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Rivaroxaban

- Einstein Jr Trial:
  - A randomized, controlled, open-label, phase 3 trial of rivaroxaban vs. standard of care for treatment of VTE in children
  - 500 children were initially treated with SOC (UFH or LMWH) and then randomized (2:1) to receive oral rivaroxaban for 3 months (and an extended phase for up to 9 months)
- UNIVERSE Trial:
  - A randomized, controlled, open-label, phase 3 trial of low-dose rivaroxaban vs. aspirin for thromboprophylaxis
  - 112 children (aged 2-8 years) with single ventricle physiology who had undergone the Fontan procedure

Rivaroxaban (Einstein Jr)

	Rivaroxaban	Comparator	Hazard ratio (95% CI)
Efficacy population			
Participants assessed	335	165	..
Primary efficacy outcome	4 (1%)	5 (3%)	0·40 (0·11–1·41)
Cerebral vein and sinus thrombosis	0	1	..
Catheter-related venous thromboembolism	0	0	..
Non-catheter-related venous thromboembolism	4	4	..
Primary efficacy outcome or deterioration on repeat imaging	5 (1%)	6 (4%)	0·41 (0·12–1·36)
Primary efficacy outcome or major bleeding	4 (1%)	7 (4%)	0·30 (0·08–0·93)
Mortality	1 (<1%)	0	..
Cancer-related	1	0	..
Safety population			
Participants assessed	329	162	..
Major or clinically relevant non-major bleeding	10 (3%)	3 (2%)	1·58 (0·51–6·27)
Major bleeding	0	2 (1%)	..
Pulmonary	0	1	..
Intracranial	0	1	..
Clinically relevant non-major bleeding	10 (3%)	1 (1%)	..
Gastrointestinal	4	0	..
Urogenital	2	0	..
Skin	1	0	..
Nasal or mouth	3	1	..

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Male et al. Lancet Haematol. 2020 Jan;7(1):e18-e27.

Rivaroxaban (UNIVERSE)

Efficacy outcomes	Rivaroxaban			ASA
	Part A (N=12)	Part B (N=64)	Total (N=76)	Part B (N=34)
Primary efficacy outcome: Any thrombotic event	1 (8)	1 (2)	2 (3)	3 (9)
Ischemic stroke	0	0	0	1 (3)
Pulmonary embolism	0	1 (2)	1 (1)	0
Venous thrombosis	1 (8)	0	1 (1)	2 (6)
Arterial/intracardiac thrombosis	0	0	0	0

Bleeding events	Rivaroxaban		ASA
	Part A (N=12)	Part B (N=64)	Part B (N=34)
Participant with ≥1 on-treatment bleeding events	4 (33)	23 (36)	14 (41)
Major bleeding	0	1 (2)	0
Clinically relevant nonmajor bleeding	1 (8)	4 (6)	3 (9)

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McCrindle et al. J Am Heart Assoc. 2021 Nov 16;10(22):e021765.

Rivaroxaban

ADULT DATA	PEDIATRIC DATA	FDA PED APPROVAL
Adult Approval since 2011 Afib, VTE tx, VTE ppx, CAD	**EINSTEIN-JR trial published 2020** Similar to SOC for tx of VTE and prevention of recurrent VTE **UNIVERSE trial published 2021** Similar to ASA for VTE ppx (low dose) in Fontan patients	Approved in December 2021 for children of all ages (weight >2.6kg)

DOSAGE FORMS

Notes

- More frequent dosing in younger patients
- Need to give with food
- Oral suspension widely available
- Andexanet alfa for reversal (no peds data)

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Apixaban

- PREVAPIX-ALL Trial:
  - A randomized, controlled, open-label, phase 3 trial of apixaban vs. no anticoagulation for prevention of VTE in children newly diagnosed with ALL during Induction
  - 512 children were randomized (1:1) to receive oral apixaban for 28 days
- SAXOPHONE Trial:
  - A randomized, controlled, open-label, phase 2 trial of apixaban vs. SOC for thromboprophylaxis in heart disease
  - 192 children (aged 28 days to 18 years) randomized (2:1) to receive full-dose apixaban for 1 year

Apixaban

- CANINES Trial:
  - A randomized, controlled, open-label, phase 3 trial of Apixaban vs. standard of care for treatment of VTE in children
  - 229 children were randomized (2:1) to receive oral apixaban for 3 months
  - Trial completed, submitted to FDA, not published yet

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Apixaban

- SAXOPHONE Trial

Efficacy

There were no thromboembolism-related deaths or thromboembolic events detected by imaging or clinical diagnosis in either treatment arm during the study.

	Apixaban (n = 126)	VKA/LMWH (n = 62)	Apixaban Difference From VKA/LMWH	Relative Risk[a]
Composite of major and CRNM bleeding	1[b] (0.8) (0.0 to 4.3)	3 (4.8) (1.0 to 13.5)	−4.0 (−12.8 to 0.8)	N/E (N/E to N/E)
Major bleeding	1 (0.8) (0.0 to 4.3)	1 (1.6) (0.0 to 8.7)	−0.8 (−8.1 to 3.3)	N/E (N/E to N/E)
CRNM bleeding	1 (0.8) (0.0 to 4.3)	2 (3.2) (0.4 to 11.2)	−2.4 (−10.5 to 1.9)	N/E (N/E to N/E)
All bleeding	47 (37.3) (28.9 to 45.8)	23 (37.1) (25.1 to 49.1)	0.2 (−14.5 to 14.9)	1.0 (0.7 to 1.5)

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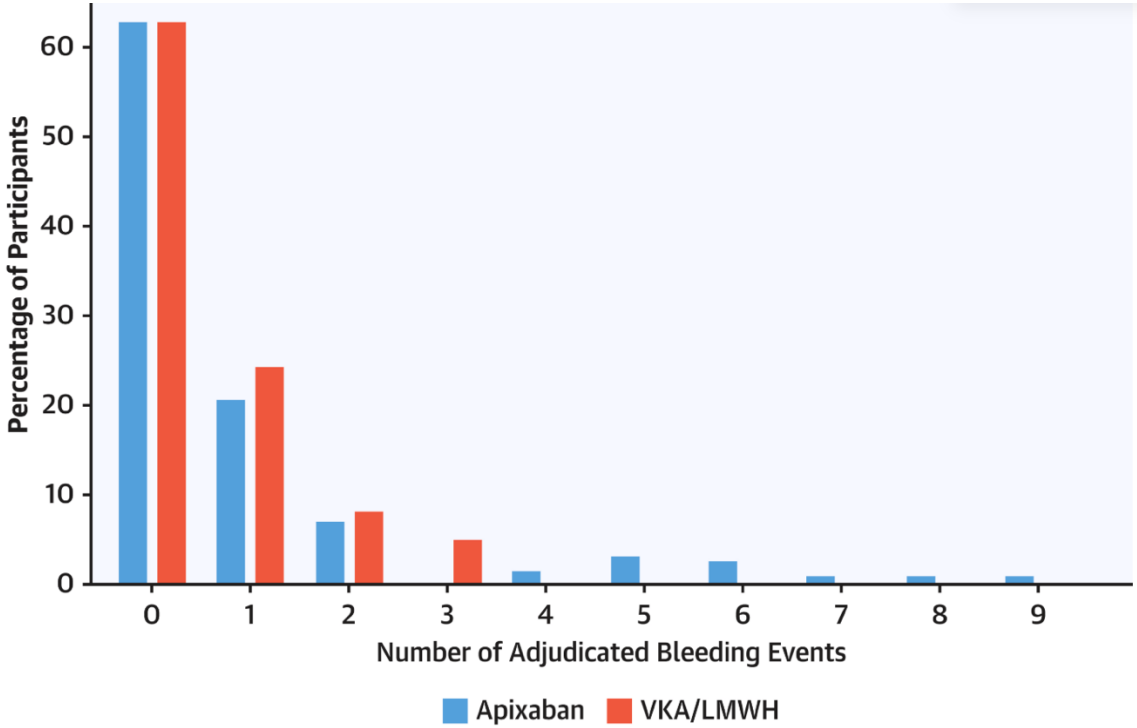
Payne et al. J Am Coll Cardiol. 2023 Dec 12;82(24):2296-2309.

Apixaban



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Payne et al. J Am Coll Cardiol. 2023 Dec 12;82(24):2296-2309.

Apixaban

ADULT DATA	PEDIATRIC DATA	FDA PED APPROVAL
Adult Approval since 2014 Afib, VTE tx, VTE ppx	**PREVAPIX-ALL published 2024** No benefit over SOC for VTE ppx (low dose) in ALL **SAXOPHONE published 2023** Similar to SOC for VTE ppx (full dose) in cardiac dz **CANINES completed enrollment** Full dose VTE treatment	Approved in April 2025 for children of all ages (weight >2.6kg) (CANINES data submitted to FDA, but not published yet)

DOSAGE FORMS

Tablet for oral suspension and sprinkle capsules coming soon!

Notes

- Twice daily dosing
- Does not require food, least renal clearance
- Andexanet alfa for reversal (no peds data)

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Anticoagulation

- Current State
  - DOACs have largely replaced warfarin as maintenance anticoagulants in the outpatient setting
- Future State
  - Studies exploring new targets, like Factor 11 inhibitors, including monoclonal antibodies (subcutaneous, once monthly dosing)

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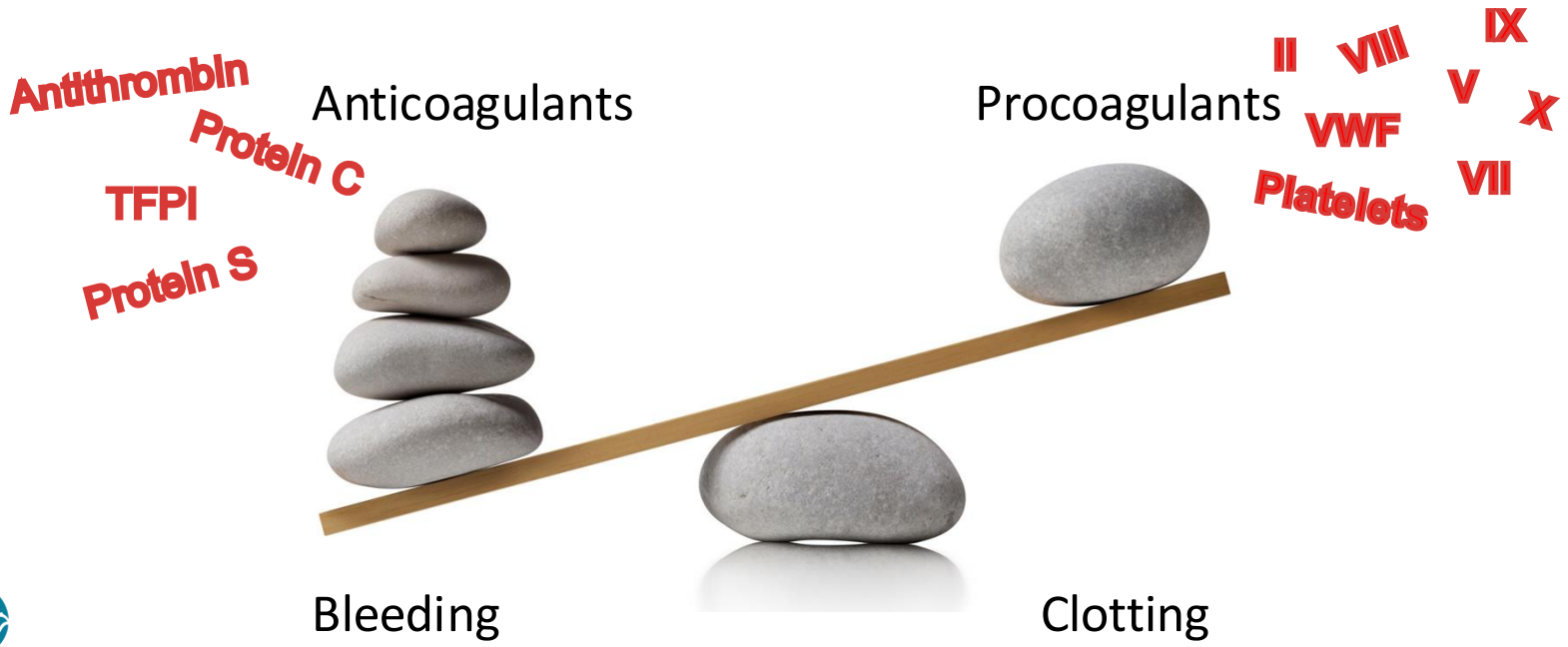
Hemophilia

- Hemophilia A
  - Congenital deficiency of clotting Factor 8
  - Mutation on X chromosome
  - 1 in 5,000 male births

- Hemophilia B
  - Congenital deficiency of clotting Factor 9
  - Mutation on X chromosome
  - 1 in 20,000 male births

Hemophilia



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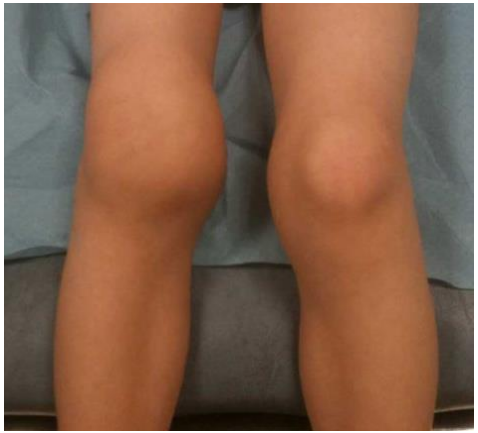
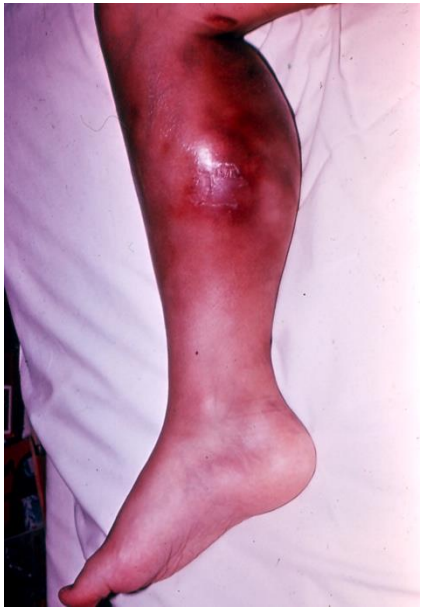
Hemophilia

- Large, deep bruises
- Prolonged bleeding from cuts, injuries
- Bleeding after dental procedures, surgeries
- Prolonged, frequent nose bleeding
- Joint bleeding
- Muscle bleeding





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Hemophilia

- Treatment: Factor Concentrates
  - Replaces the missing factor
  - Powder that requires reconstitution with water
  - Administered by IV infusion
  - “Standard half-life” products require frequent infusions
    - At least daily infusions for bleeds
    - Factor 8: three times per week for prevention
    - Factor 9: two times per week for prevention

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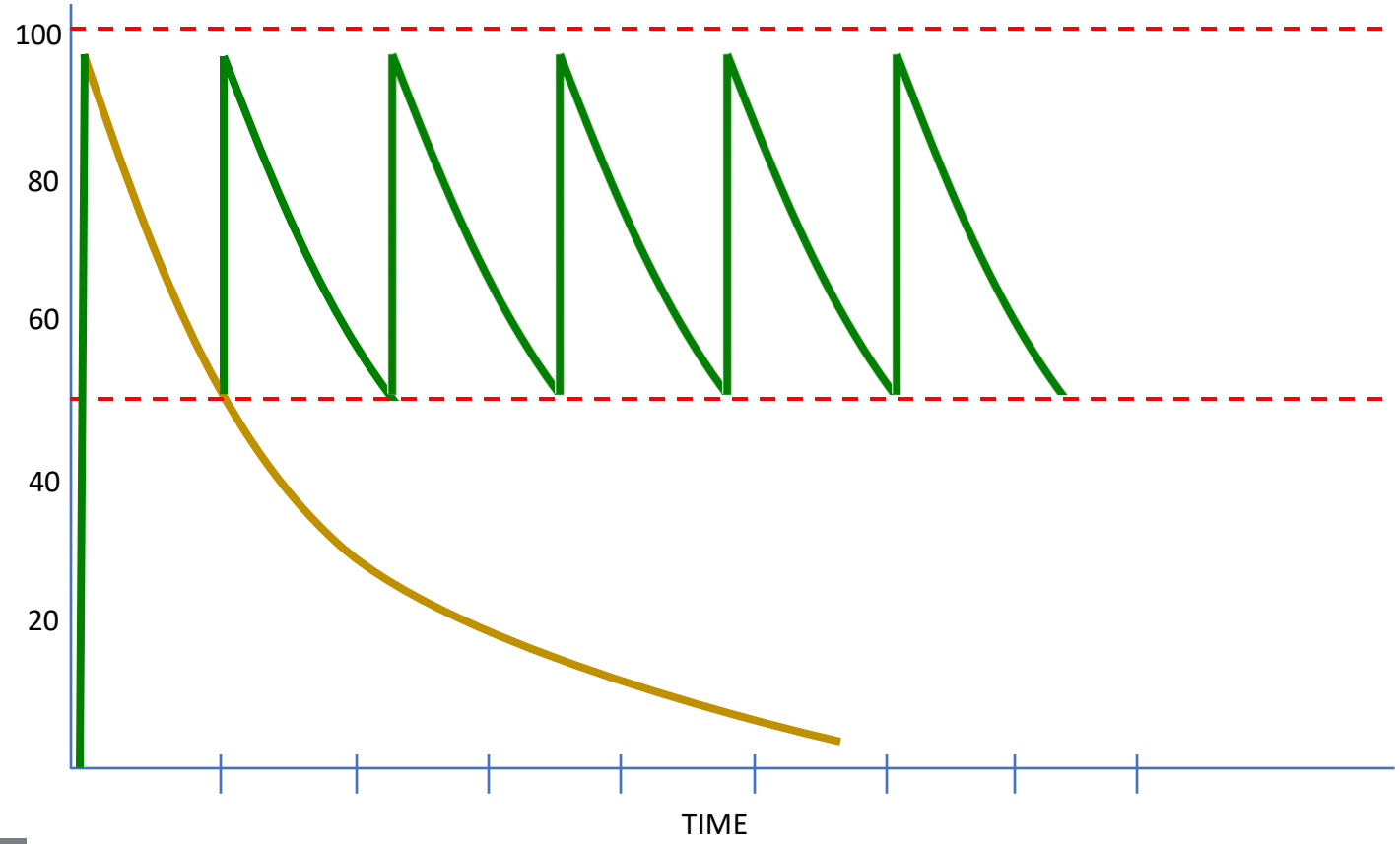
Hemophilia



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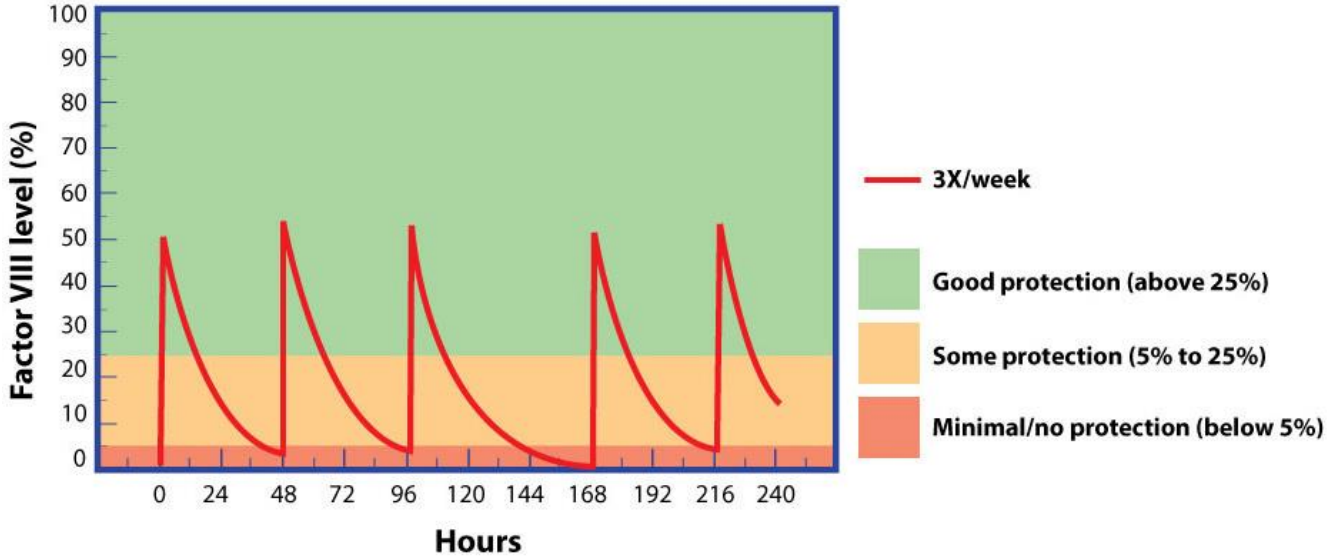
Hemophilia

Prevention



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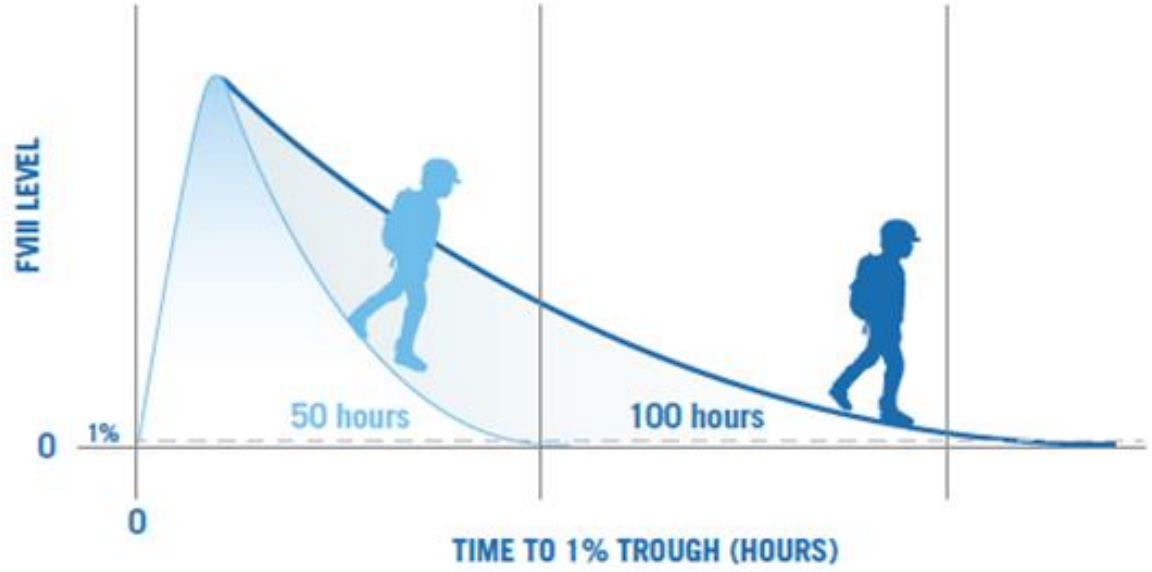
Hemophilia

- Treatment: Extended Half-Life Factor



Fc Fusion
Directs Factor away From the lysosome

Albumin Fusion
Stabilizes Factor in the circulation

GlycoPEGylation
Reduces renal clearance, prolongs circulation time, masks from host immune system, adds water solubility

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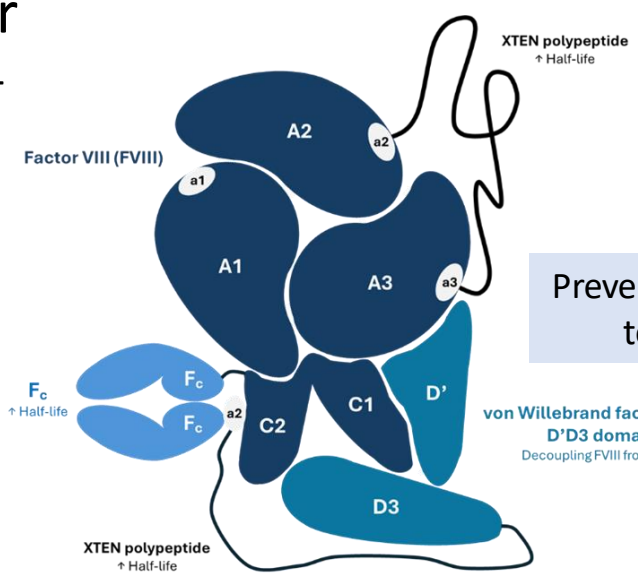
Hemophilia

- Treatment: Extended Half-Life Factor
  - We now have F8 and F9 products with half-lives long enough to allow once weekly infusions for prophylaxis

Slows clearance & prevents enzymatic breakdown



Prevents binding to VWF

Prolongs circulation

EFANESOCTOGOC ALFA

rFVIIIFc-VWF-XTEN

fusion protein

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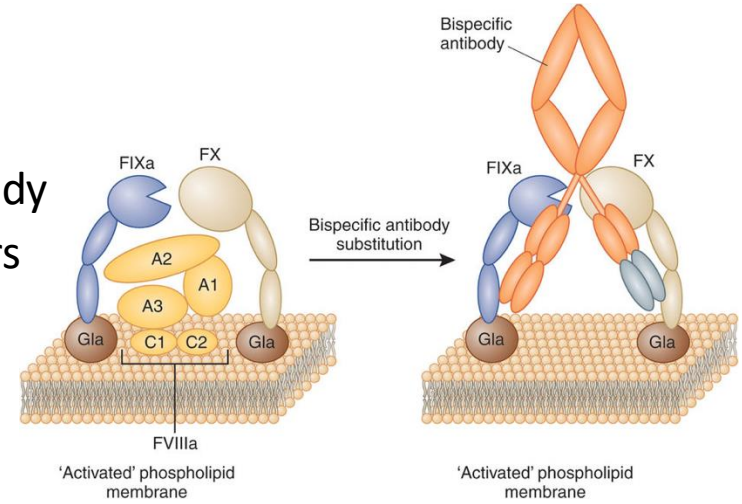
Hemophilia

- Treatment: Factor Mimetics
  - Do not replace the missing factor
  - Monoclonal antibodies
  - Administered by subcutaneous injection
  - Injections can be once every 1, 2, or 4 weeks

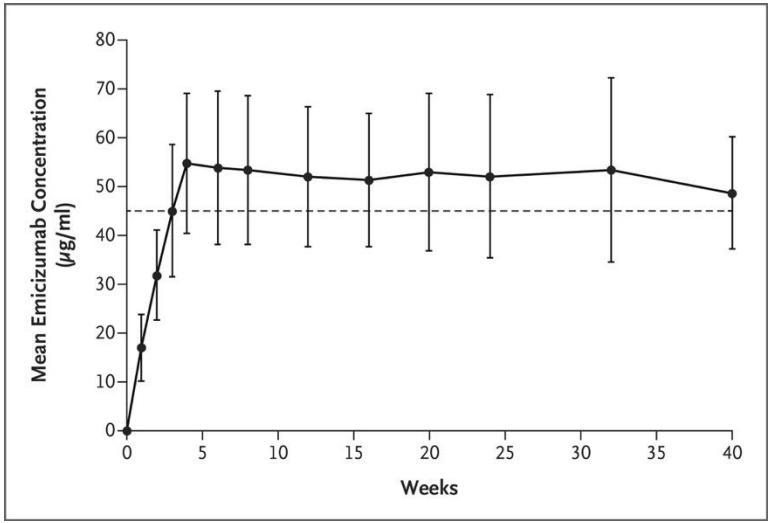
- Emicizumab (Hemlibra- 2017)
  - Bispecific Factor 9a and Factor 10 directed antibody
  - Used only in Hemophilia A with/without inhibitors



Seattle Children's

Hemophilia

- Treatment: Factor Mimetics
  - Long half-life, stable levels
  - Factor 8 equivalence can be estimated by thrombin generation
  - Likely 15-30% F8 activity
  - Patients will still need factor infusions for injuries/surgeries



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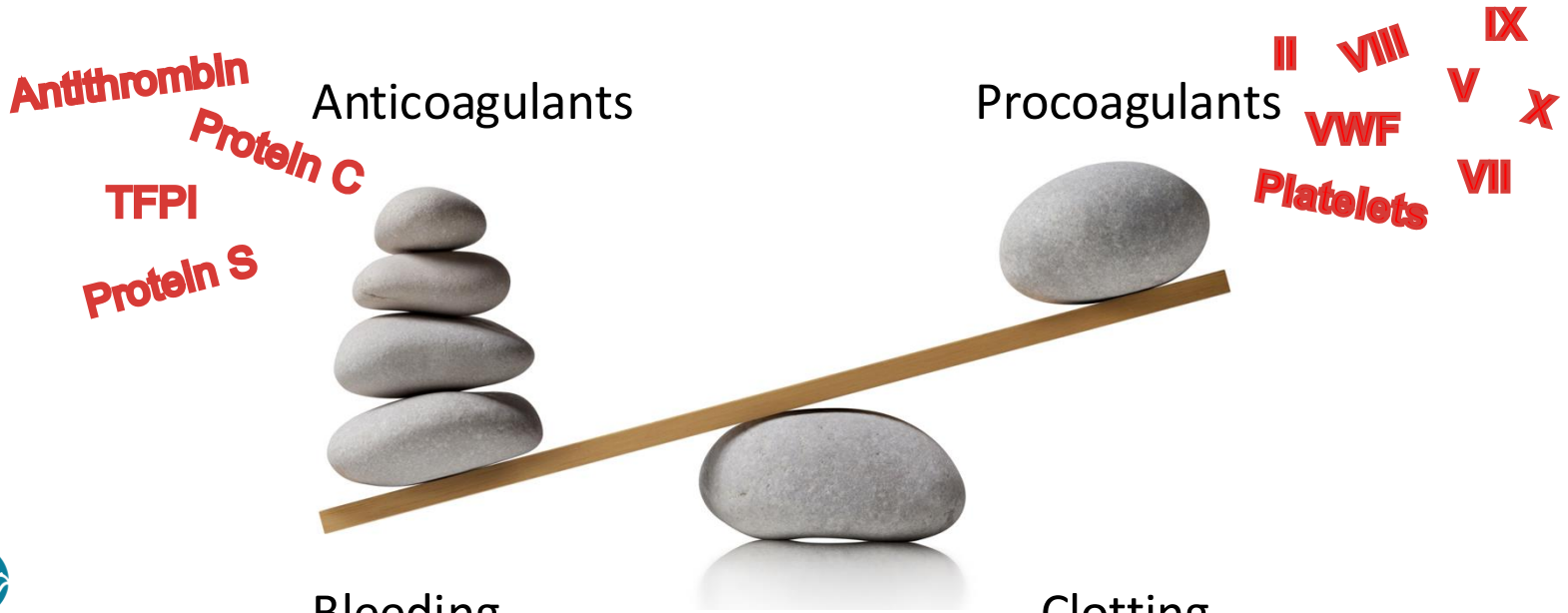
Hemophilia

- Treatment: Rebalancing Agents



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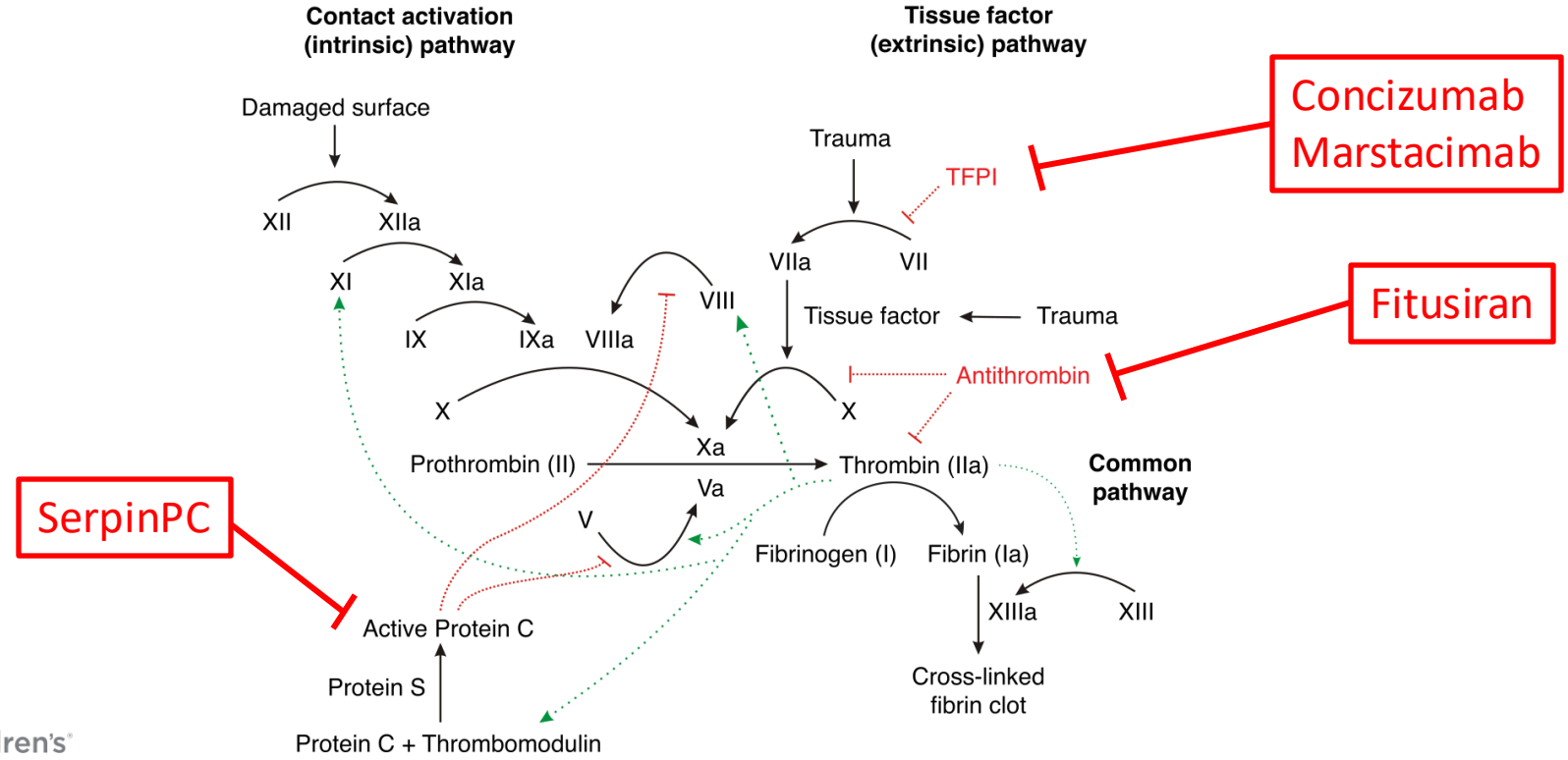
Rebalancing Agents



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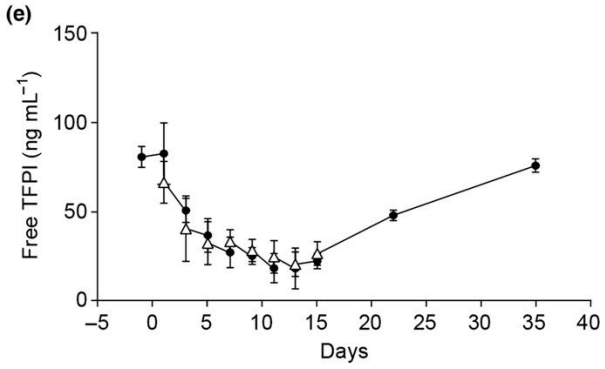
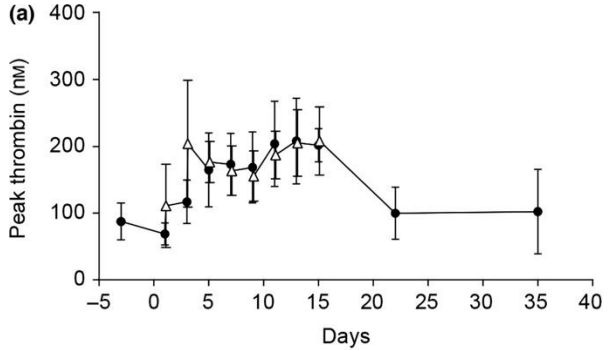
Concizumab (Alhemo- 2024)

- Monoclonal antibody against Tissue Factor Pathway Inhibitor (TFPI)
- Approved for ≥ 12 years old with Hemophilia A or B
- Daily subcutaneous injections for prophylaxis
- Effective for patients with or without inhibitors
- Thromboembolic events reported in clinical trials





Haemophilia. 2017 Sep;23(5):769-776.

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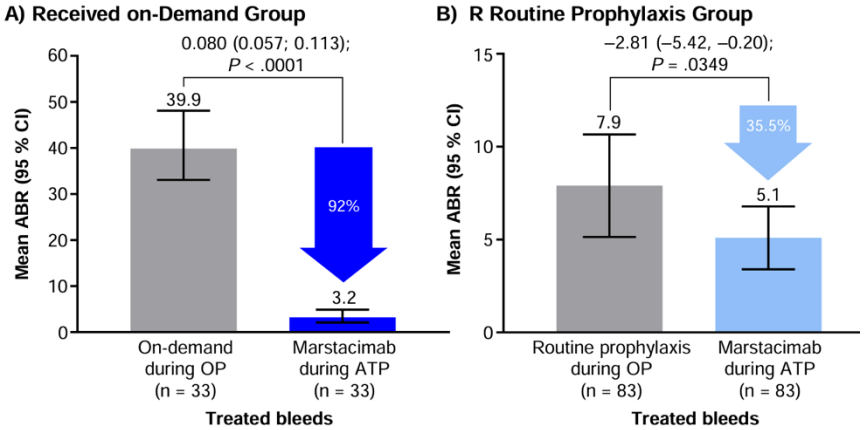
Marstacimab (Hympavzi- 2024)

- Monoclonal antibody against Tissue Factor Pathway Inhibitor (TFPI)
- Approved for ≥ 12 years old with Hemophilia A or B
- Weekly subcutaneous injections for prophylaxis
- Effective for patients with or without inhibitors



Phase 3 BASIS Trial
- 116 males age 12 to 75
- Severe Hem A or B
- No inhibitors
- 12 months
- No TE events

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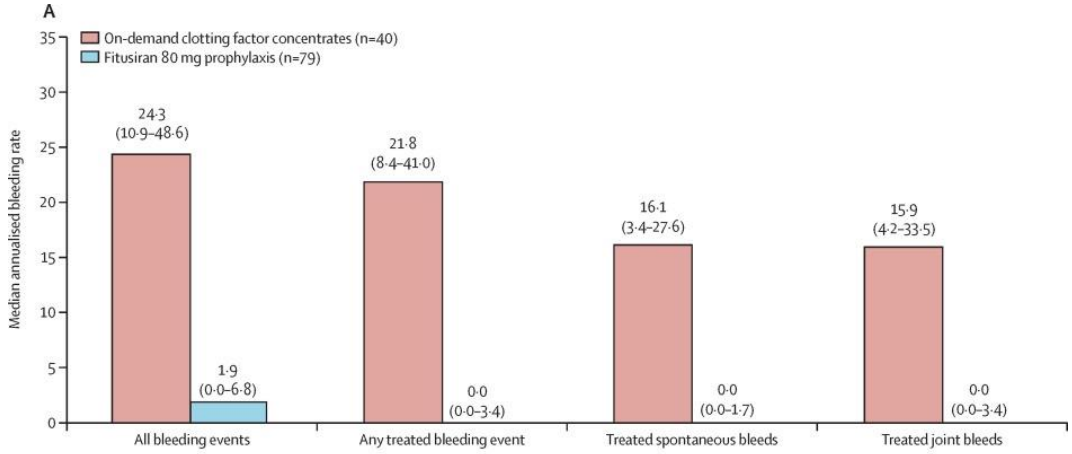
Blood. 2025 Jul 3:blood.2024027468. Epub ahead of print.

Fitusiran (Qfitlia- 2025)

- Interfering RNA that causes degradation of Antithrombin mRNA
- Approved for ≥ 12 years old with Hemophilia A or B with or without inhibitors
- Every two-month subcutaneous injections for prophylaxis
- Thromboembolic events reported in clinical trials
- Must measure Antithrombin levels (maintain between 15-35%)



Lancet Haematol. 2023 May;10(5):e322-e332.

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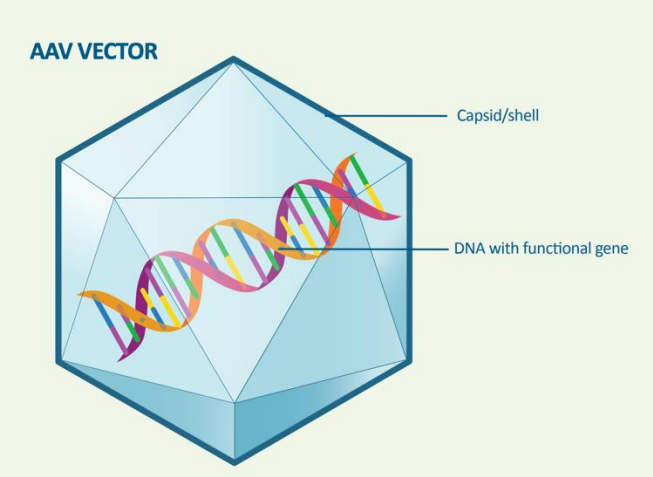
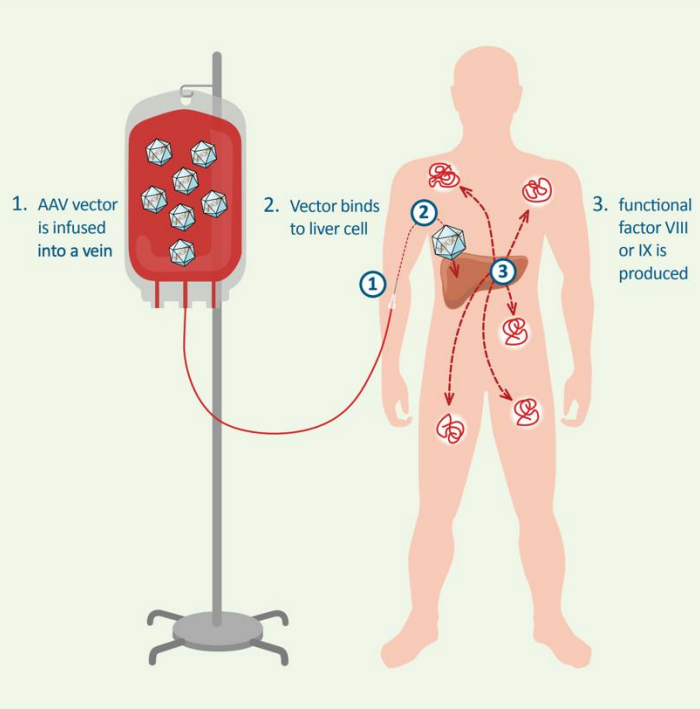
Hemophilia

- Treatment: Gene Therapy





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Gene Therapy

- Pros
  - Single infusion
  - No chemo
  - Normal F8 or F9 levels
  - Effective- reduces bleeds
  - No need for prophylaxis
  - Improved QOL
- Cons
  - Some patients excluded
  - Variability in levels
  - Immune response- steroids
  - Durability questions
  - Redosing not possible
  - Expensive

Gene Therapy

- Many clinical trials
- Two currently approved commercial infusions
  - Valoctocogene roxaparvovec (Roctavian)- Hem A
    - Approved 2023 (adults only)
  - Etranacogene dezaparvovec (Hemgenix)- Hem B
    - Approved 2022 (adults only)
  - Fidanacogene elaparvovec (Beqvez)- Hem B
    - Pulled off market by Pfizer Feb 2025
    - Pfizer cited low patient & provider interest

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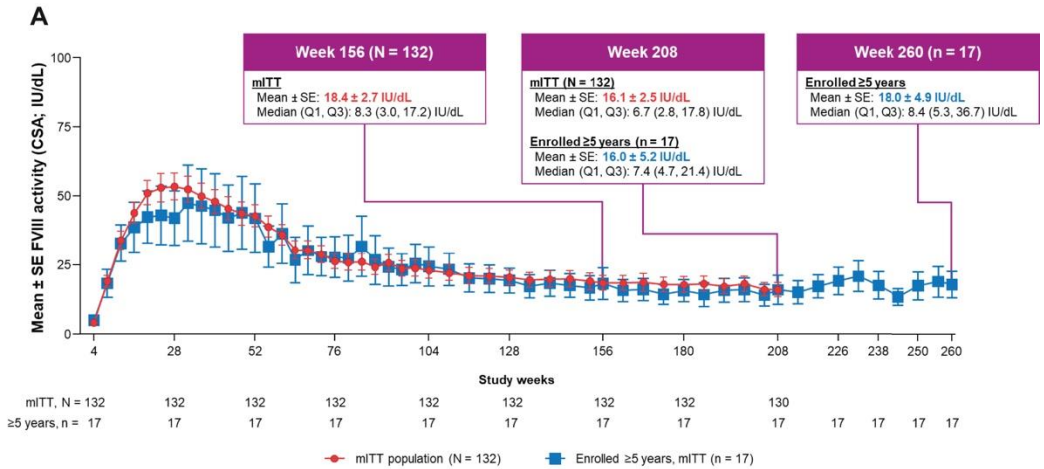
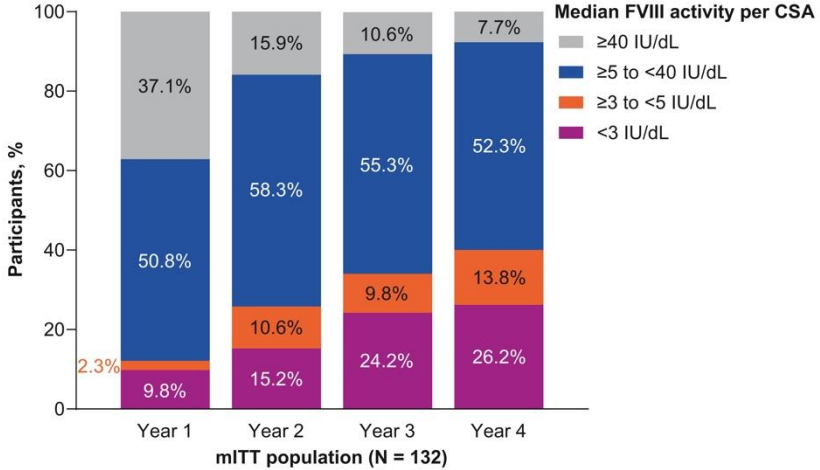
Valoctocogene roxaparvovec (Roctavian)





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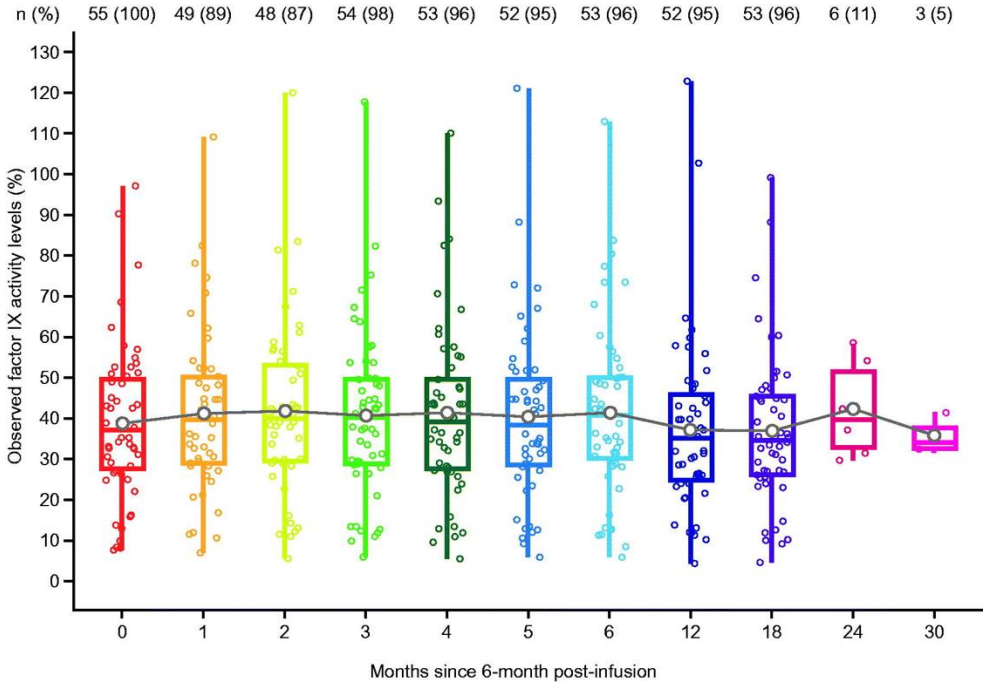
Res Pract Thromb Haemost. 2024 Oct 30;8(8):102615.

Etranacogene dezaparvovec (Hemgenix)



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Curr Med Res Opin. 2023 Feb;39(2):227-237.

Hemophilia

- Current State
  - Most patients with Hem A are on emicizumab
  - Most patients with Hem B are on EHL factor
  - Some patients beginning to try rebalancing agents
  - Some adults receiving gene therapy
- Future State
  - Gene therapy holds much promise if the durability can be guaranteed

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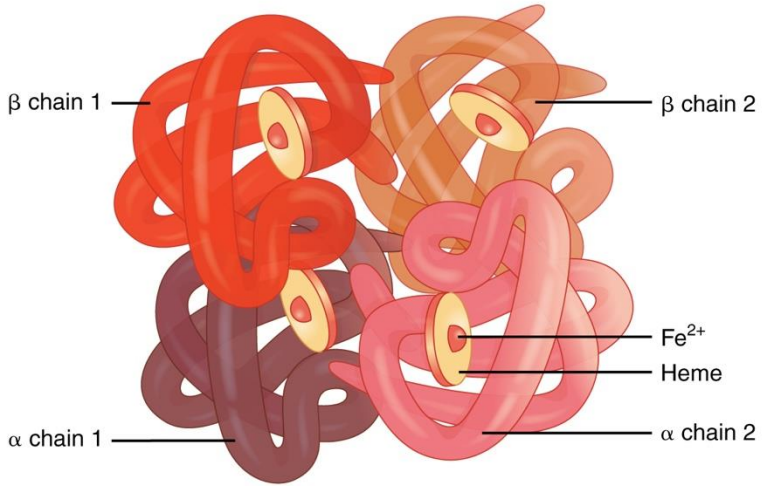
Hemoglobinopathies

- Genetic disorders of hemoglobin
  - May affect structure or function
    - Reduced production
    - Molecules with altered affinity for oxygen
    - Unstable molecules
    - Misshapen molecules



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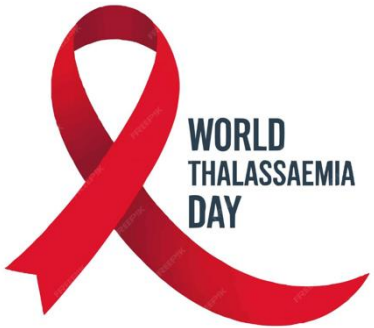
Thalassemia

- Many different mutations that can affect alpha or beta globin chain production
- Decreased effective production of hemoglobin
- Wide spectrum of clinical disease
  - “silent carrier” to “hydrops fetalis”
  - Microcytic anemia
  - Some are transfusion-dependent
    - High burden of care

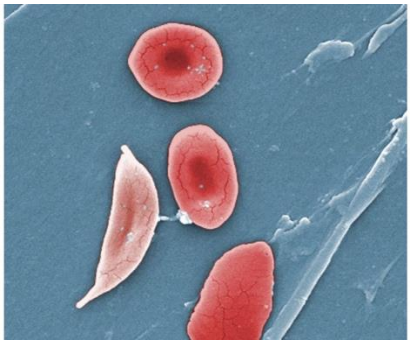


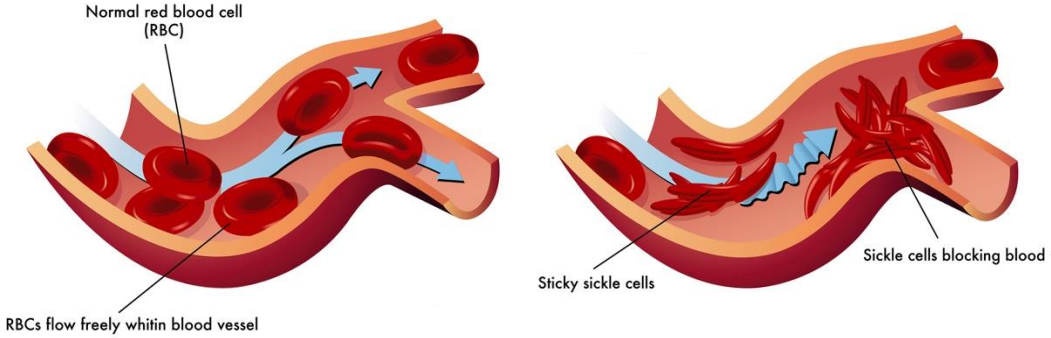
Long-term complications

- Iron overload
- Bone deformities
- Endocrinopathies
- Delayed growth
- Delayed puberty
- Thrombophilia
- Hypersplenism

Sickle Cell Disease

- A specific genetic point mutation in the sickle cell gene causes hemoglobin to behave abnormally
- Under conditions of low oxygen the hemoglobin molecules “stick” together forming long, rigid strands
- These strands stretch out the cell into its characteristic shape





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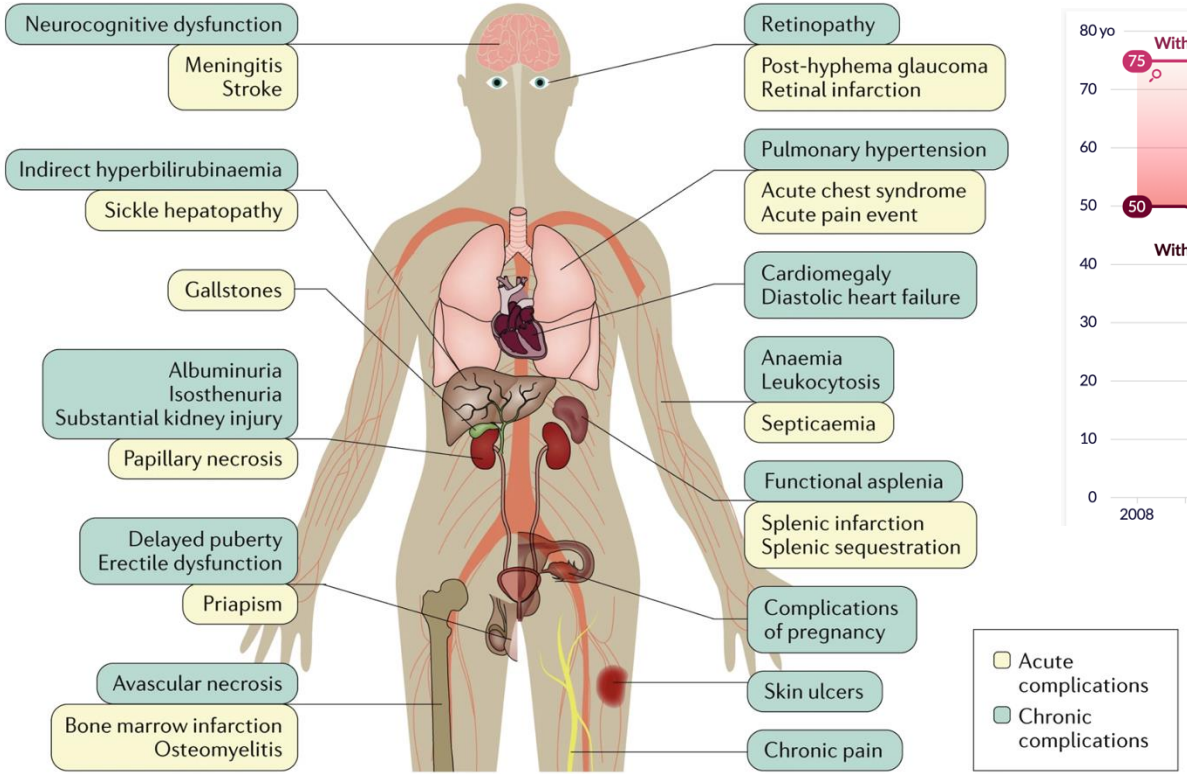
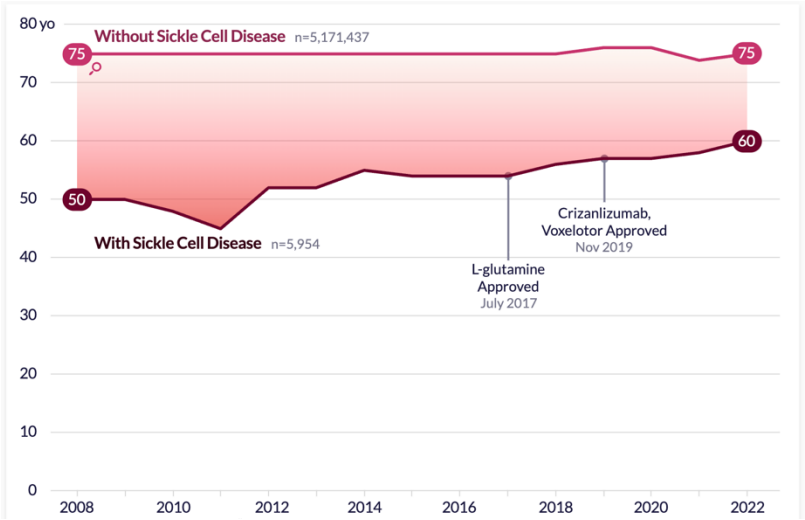
Sickle Cell Disease





Nat Rev Dis Primers. 2018 Mar 15;4:18010.

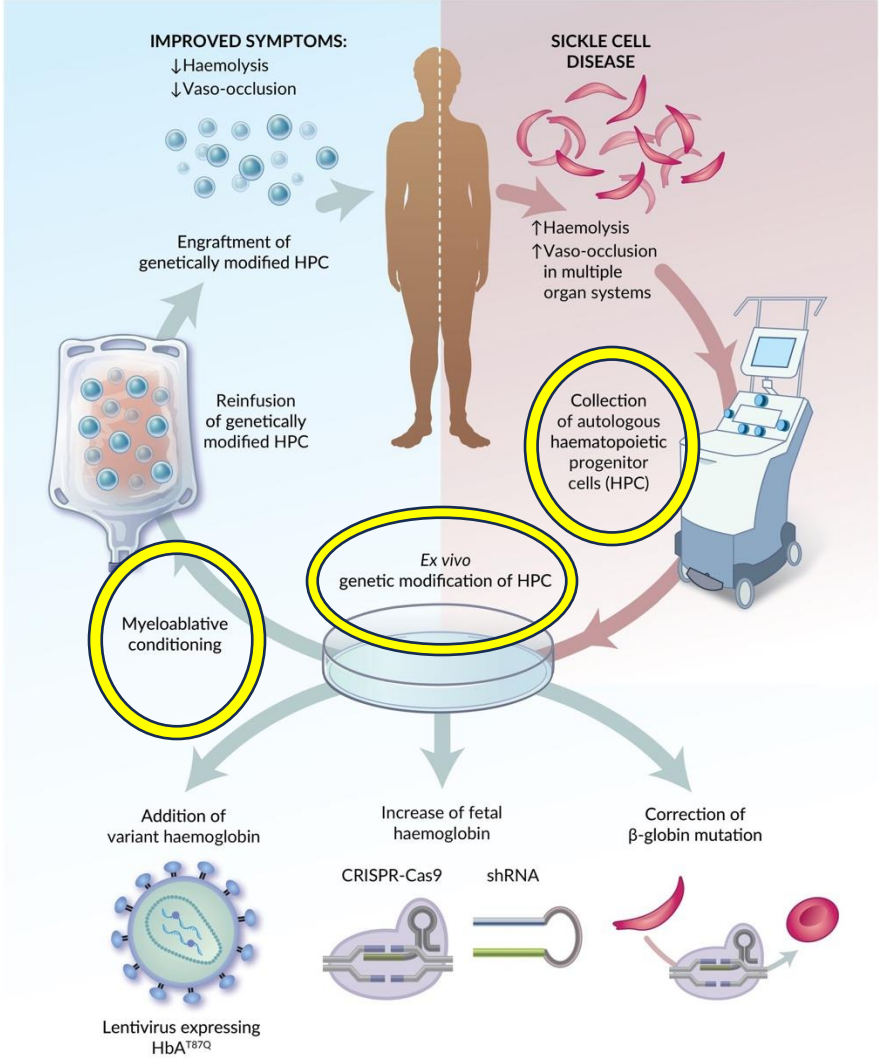
Gene Therapy

Risks of Gene Therapy

Collection:
- Need to stop other medicines

Gene Modification:
- Insertional oncogenesis
- Off-target gene editing

Conditioning:
- Infertility
- Chemo side effects (mucositis)
- Weakened immune system
- Infections



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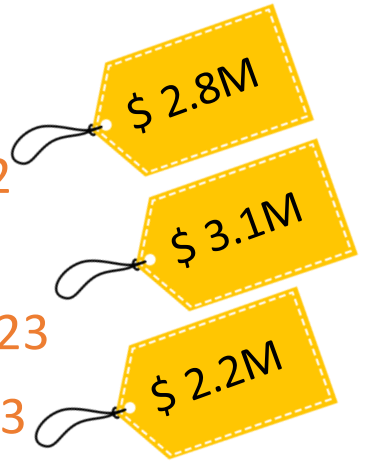
Vox Sang. 2024 Jun;119(6):521-528.

Gene Therapy

- Three products currently on the market
- Thalassemia
  - Betibeglogene autotemcel (Zynteglo)- 2022
- Sickle Cell Disease
  - Lovotibeglogene autotemcel (Lyfgenia)- 2023
  - Exagamglogene autotemcel (Casgevy)- 2023



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Betibeglogene autotemcel (Zynteglo)

- Open label, phase 3, single group study
- Autologous CD34+ hematopoietic stem and progenitor cells transduced with the BB305 lentiviral vector encoding the β-globin (βA-T87Q) gene (Bluebird Bio)
- 23 patients with TDT
- Median follow-up 30 months
- Primary efficacy end point- transfusion independence

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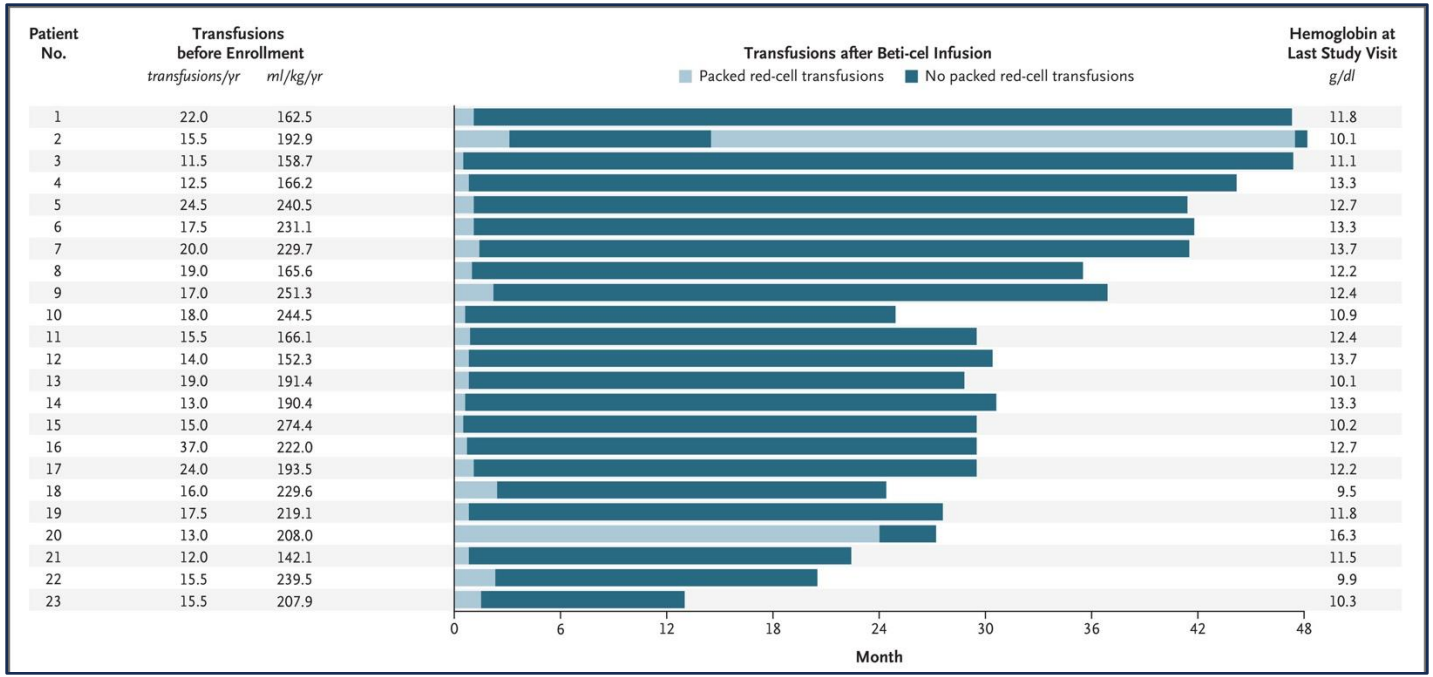
Betibeglogene autotemcel (Zynteglo)



Efficacy

20/22 (91%) subjects were transfusion-independent for ≥ 12 months

Safety

Replication-competent lentivirus, clonal predominance, and insertional oncogenesis were not detected.

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N Engl J Med. 2022 Feb 3;386(5):415-427.

Lovotibeglogene autotemcel (Lyfgenia)

- Open label, phase 1-2, single group study
- Autologous CD34+ hematopoietic stem and progenitor cells transduced with the BB305 lentiviral vector encoding the β-globin (βA-T87Q) gene (Bluebird Bio)
- 35 patients with SCD
- Median follow-up 17 months
- Primary efficacy end point- complete resolution of severe vaso-occlusive events, measured between 6 and 18 months after the LentiGlobin infusion

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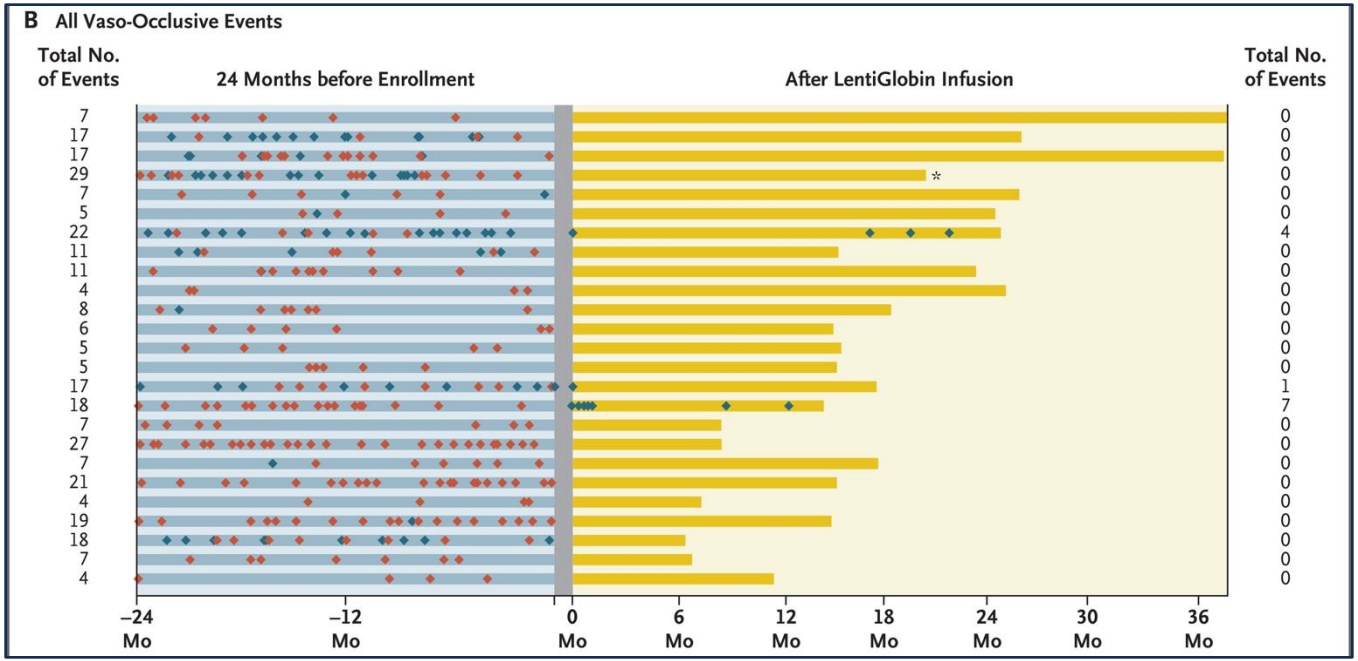
Lovotibeglogene autotemcel (Lyfgenia)



Efficacy

25/25 (100%) subjects had resolution of severe vaso-occlusive events

Safety

One death from cardio-pulmonary disease

Replication-competent lentivirus, clonal predominance, and insertional oncogenesis were not detected.

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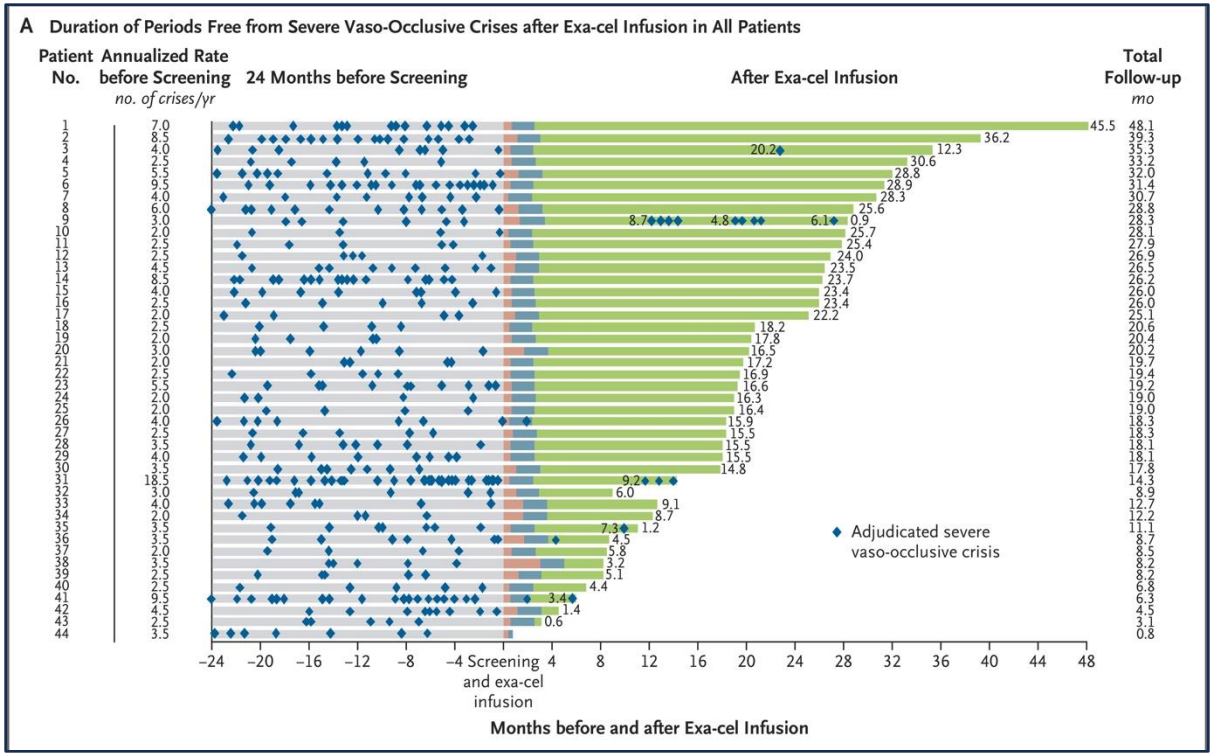
N Engl J Med. 2022 Feb 17;386(7):617-628.

Exagamglogene autotemcel (Casgevy)

- Open label, phase 3, single group study
- CRISPR–Cas9 gene editing of autologous CD34+ hematopoietic stem and progenitor cells at the erythroid-specific enhancer region of BCL11A (Vertex)
- 44 patients with SCD
- Median follow-up 19 months
- Primary efficacy end point- complete resolution of severe vaso-occlusive events for at least 12 consecutive months

Exagamglogene autotemcel (Casgevy)



Efficacy

29/30 (97%) subjects had resolution of severe vaso-occlusive Events for 12 months

Safety

One death from COVID and preexisting lung disease

No cancers were detected.

Additional studies being performed to evaluate for any potential off-target editing.

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N Engl J Med. 2024 May 9;390(18):1649-1662.

Hemoglobinopathies

- Current State
  - The results of gene therapy trials are very promising
  - Patients who meet clinical criteria are being offered commercial gene therapy at select centers
  - We are working with payors to get these therapies covered
- Future State
  - Gene therapy holds much promise, competitors are likely to gain approval in the coming months
  - The key to making gene therapy safer for this population would be non-toxic conditioning regimens

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Summary

- Hematology, as a field, is changing rapidly
- Advances in research and a deeper understanding of molecular pathways have made this an exciting time in benign hematology
- Breakthroughs in disease-specific medications, targeted therapy, and gene therapy are transforming the treatment landscape for inherited and acquired blood disorders

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