A grayscale photograph of a modern, multi-story building with a glass facade and a curved brick base. The building is identified as the Emily Couric Clinical Cancer Center. The text "EMILY COURIC CLINICAL CANCER CENTER" is visible on the brick base. The building is surrounded by trees and a paved area.

Challenging Cases in Classical Hematology

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Disclosures

- Sanofi
- Sobi

Case 1

- Ms. A: 57 yo woman with metastatic HR+/HER2+ breast cancer metastatic to the brain. She comes in for her Enhertu infusion and complains of right calf pain and swelling.







































Case 1

Impression

1. Occlusive noncompressible expansile acute appearing thrombus within the right common femoral vein extending into the proximal greater saphenous vein and proximal femoral vein.
2. No evidence of left lower extremity DVT from the level of the common femoral vein through the calf.

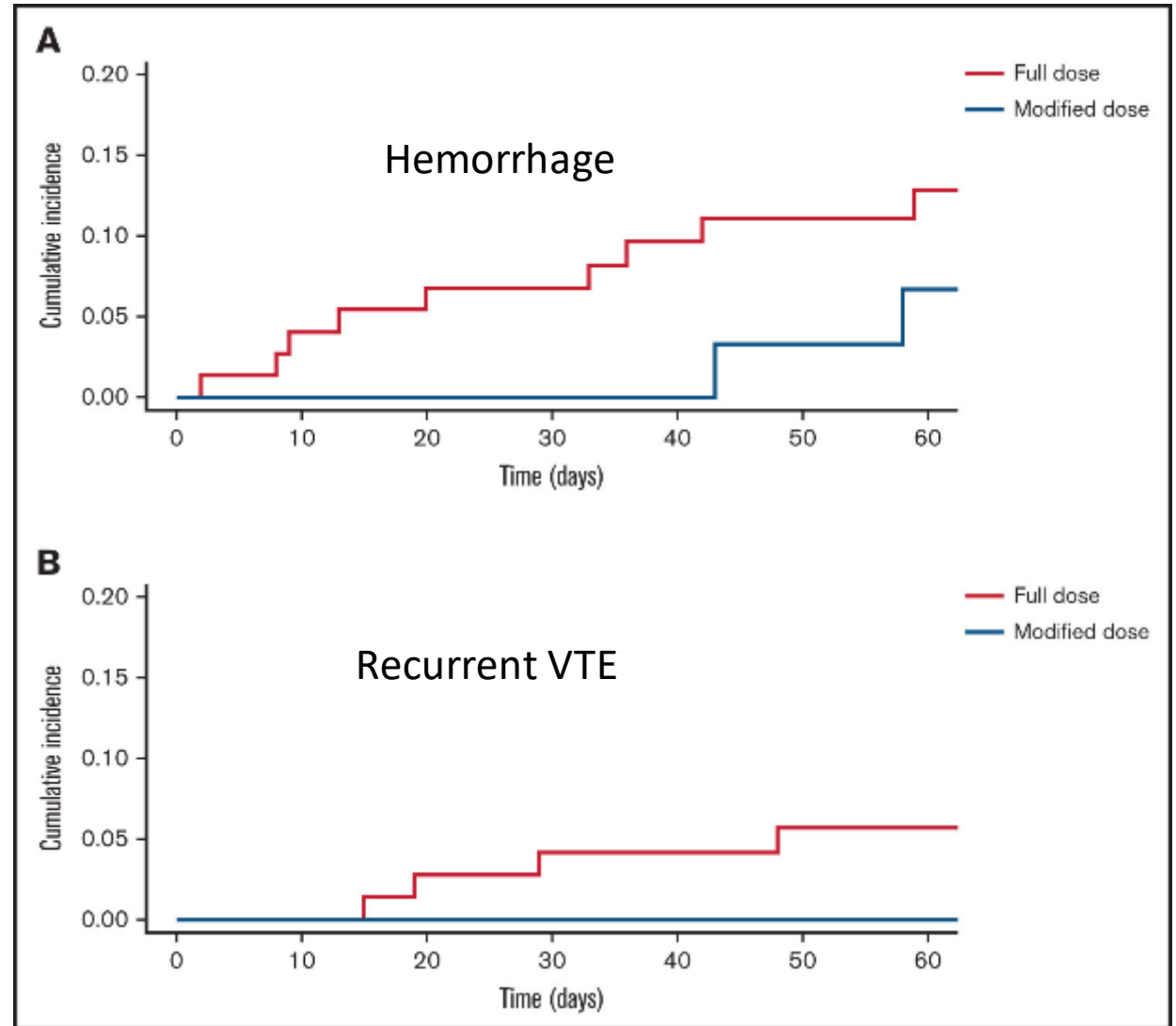
Case 1

- DVT in R common femoral vein extending into the proximal veins

COMPLETE BLOOD CO... 		
WBC	9.66 	10.88 
RBC	3.34  	3.14  
Hemoglobin	9.2  	8.6  
Hemoglobin (Chem)		
Hematocrit	29.7  	27.6  
Hematocrit (Chem)		
MCV	88.9 	87.9 
MCH	27.5  	27.4  
MCHC	31.0  	31.2  
RDW	14.5  	14.4  
Platelets	44  	53 
MPV	10.8 	10.7 
Nucleated RBC Percent	1 	1 
Nucleated RBC Abs	0.070 	0.100 

Anticoagulation and Thrombocytopenia

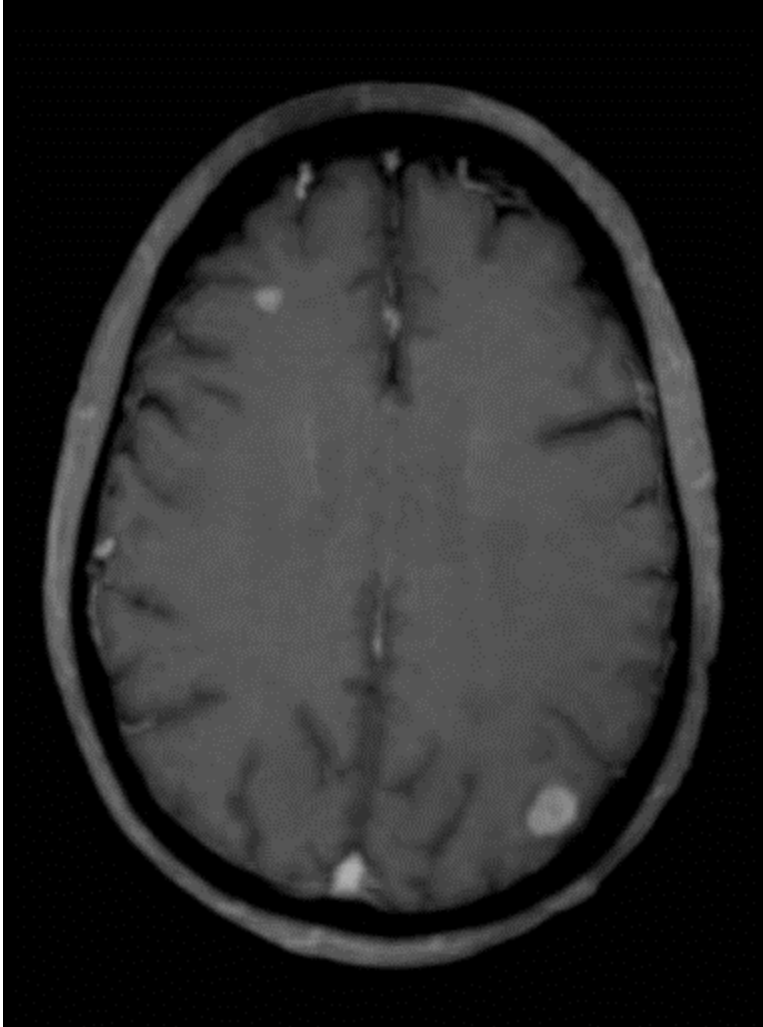
- Platelet transfusion
 - increased risk for recurrent VTE
 - Increased risk of ICH
- Better outcomes with dose modification



Anticoagulation and Thrombocytopenia

- Platelets $\geq 50 \times 10^9/L$: Therapeutic anticoagulation
- Platelets ≥ 30 but $< 50 \times 10^9/L$: 50% dose reduction
- Platelets $< 30 \times 10^9/L$: consider IVC filter

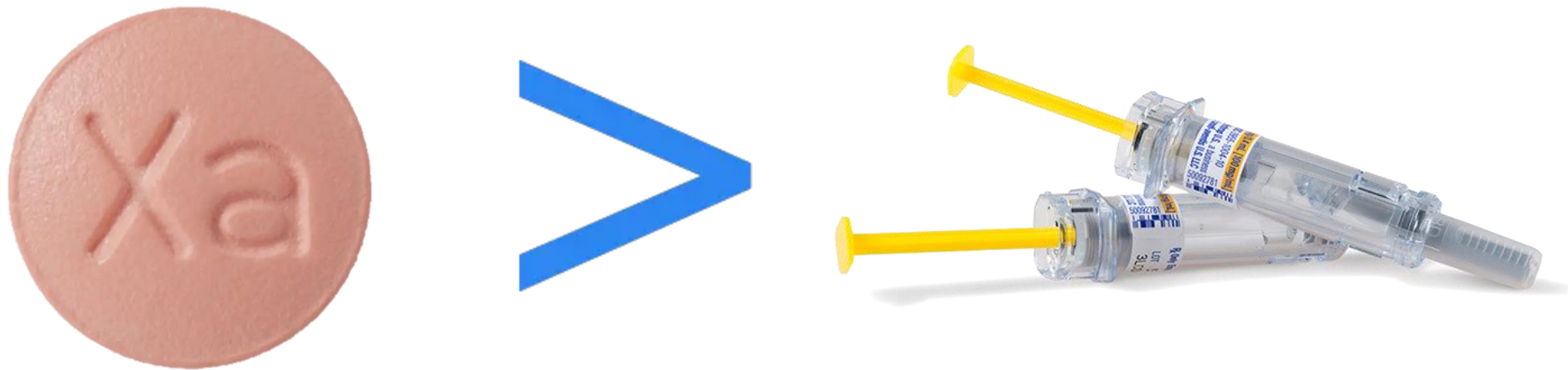
Anticoagulation and Brain Mets



- No increase in risk of ICH with anticoagulation
- Renal Cell Carcinoma and Melanoma are more likely to bleed

Which Anticoagulant?

- DOACs preferred over LMWH
 - Decrease VTE recurrence
 - Decrease major bleeding
 - GI cancers are the exception
- Indefinite anticoagulation for secondary prophylaxis





Case 1

- Ms. A has normal liver and kidney function and starts anticoagulation with rivaroxaban 20mg daily with plans to complete a 3 month course
- At 3 month follow up we drop her back to prophylactic dose rivaroxaban 10mg daily

Case 2

- Mr B is a 58yo man with thrombocytopenia in the setting of cirrhosis. He is referred for clearance prior L4 to S1 laminectomy and fusion.

COMPLETE BLOOD CO...  	
WBC	03/15/23 2.35 ▼
RBC	03/15/23 3.60 ▼
Hemoglobin	03/15/23 9.8 ▼
Hemoglobin (Chem)	08/24/17 10.5 ▼
Hematocrit	03/15/23 32.1 ▼
Hematocrit (Chem)	08/24/17 31.0 ▼
MCV	03/15/23 89.2
MCH	03/15/23 27.2 ▼
MCHC	03/15/23 30.5 ▼
RDW	03/15/23 13.2
RDW SD	09/18/17 53.8 ▲
Platelets	03/15/23 77 ▼
MPV	03/15/23 11.0
Nucleated RBC Percent	03/15/23 0
Nucleated RBC Abs	03/15/23 0.000
Protime	18.3 ▲
Protime INR	1.6 ▲

Coagulation Parameters prior to high risk procedures

	ISTH 2021	EASL 2022	AGA 2021	SIR 2019
PT/INR	Do not evaluate	Do not correct	Do not correct	Vit K for INR>2.5
Platelet count	Do not correct	Do not correct	>50× 10 ⁹ /L	>30 × 10 ⁹ /L
Fibrinogen	Do not evaluate	Do not correct	no recommendation	>1 g/L
Viscoelastic Testing	Do not evaluate	Do not evaluate	May be useful	no recommendation



Case 2



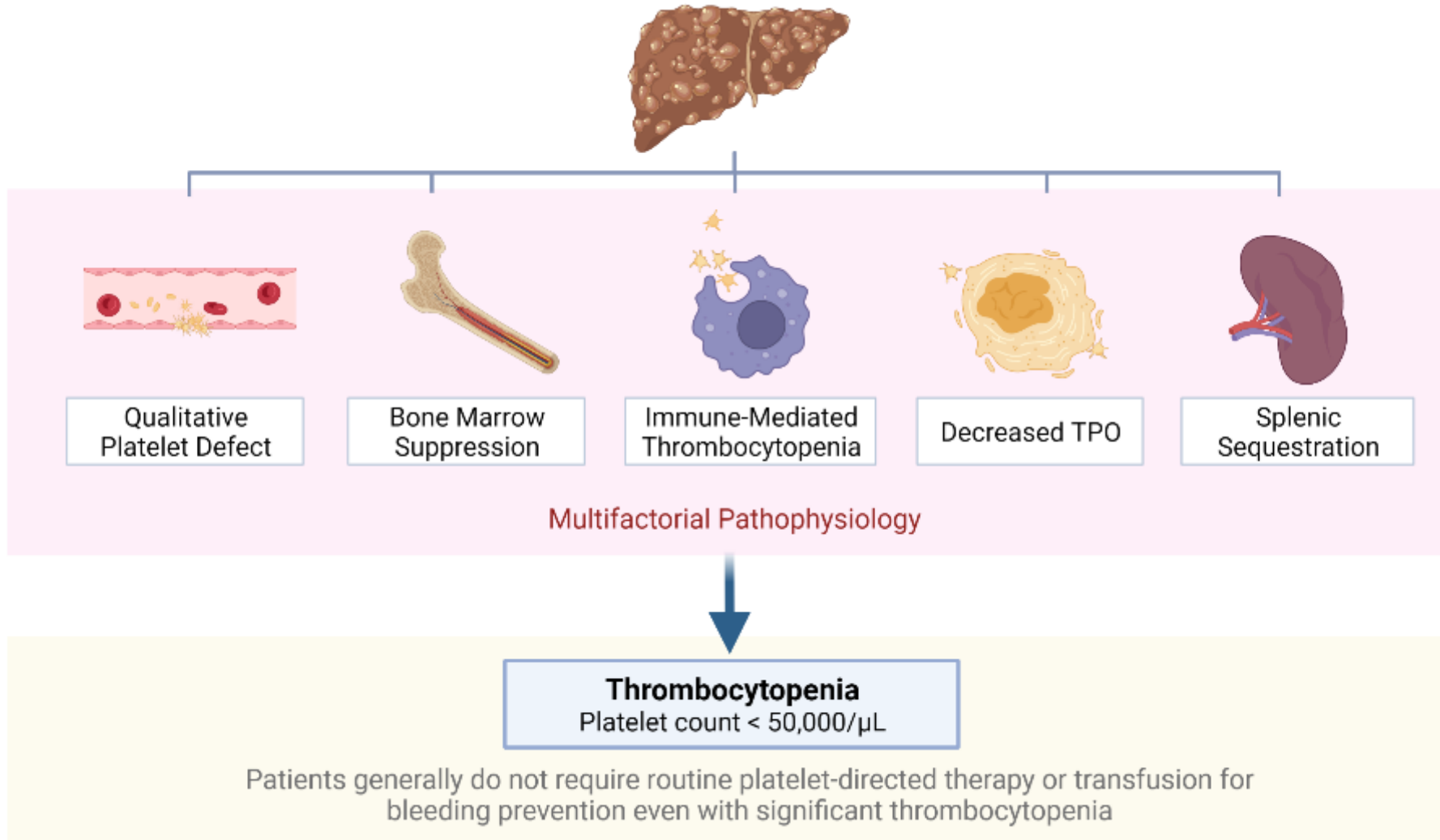
- Neurosurgery would like platelets to be >100k and INR<1.4

Replacement Products

- Low fibrinogen is not associated with abnormal bleeding, use of cryo does not improve bleeding or survival
- FFP will increase portal pressures and increase bleeding risk
- PCC and rFVII have showed poor efficacy in the treatment of bleeding
- A single 10mg dose of vitamin K may lower INR
- Antifibrinolytic therapy can be used to manage peri procedural bleeding

Thrombocytopenia

Thrombocytopenia and Thrombocytopathy in Liver Cirrhosis



Thrombocytopenia

Low-Risk Procedures

- No role for routine transfusion or TPO-RA therapy
- Consider conservative measures such as suspension of toxins or medications potentially contributing to thrombocytopenia

High-Risk Procedures

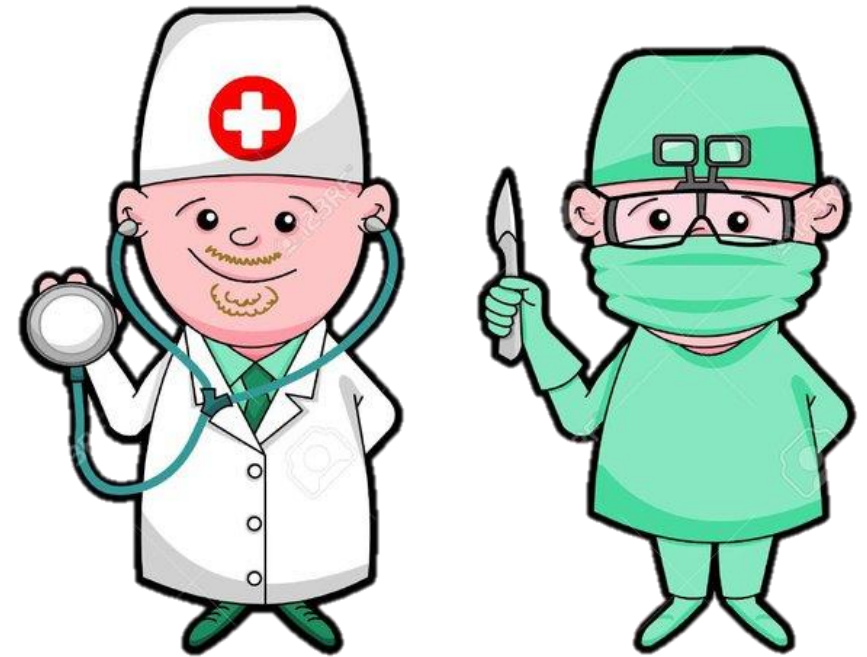
- Consider TPO-RA
 - Avatrombopag 40-60mg daily x 5 days, starting 10-13 days prior to procedure
 - Lusutrombopag 3mg daily x 7 days, starting 8-14 days prior to procedure
- Trial of ITP therapy for patients with autoimmune liver disease or HCV
- Consider transfusion if inadequate response to TPO-RA or immune thrombocytopenia treatment

Recommendations

- Look for modifiable risk factors
- For most people don't try to correct the INR
- Consider TPO-RA for very high risk procedures













Case 2

- Mr. B is currently listed for liver transplant
- Agree that $INR < 2.0$ is OK, plan to give 1g TXA
- Platelet count is > 50 so plan to have platelets on hold to the OR if bleeding



Case 3

- Ms. C is a 48yo woman with stage III Ovarian cancer getting adjuvant carbo/taxol but her chemotherapy has been repeatedly delayed by thrombocytopenia

COMPLETE BLOOD CO...  		
WBC	11:59	22.64 
RBC	11:59	2.91 
Hemoglobin	11:59	8.9 
Hemoglobin (Chem)	03/25/23	9.6 
Hematocrit 	11:59	26.1 
Hematocrit (Chem)	03/25/23	28.0 
MCV	11:59	89.7
MCH	11:59	30.6
MCHC	11:59	34.1
RDW	11:59	17.9 
Platelets	11:59	15  

Thrombocytopenia in the Cancer Patient



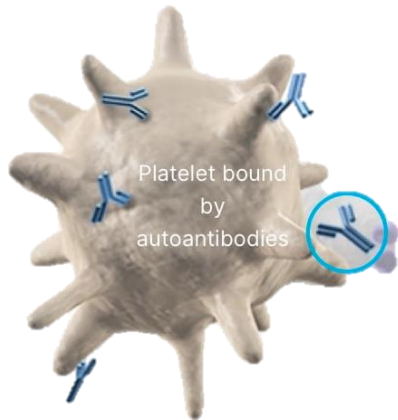
Bone Marrow infiltration



Viral or bacterial infection



Post transfusion purpura



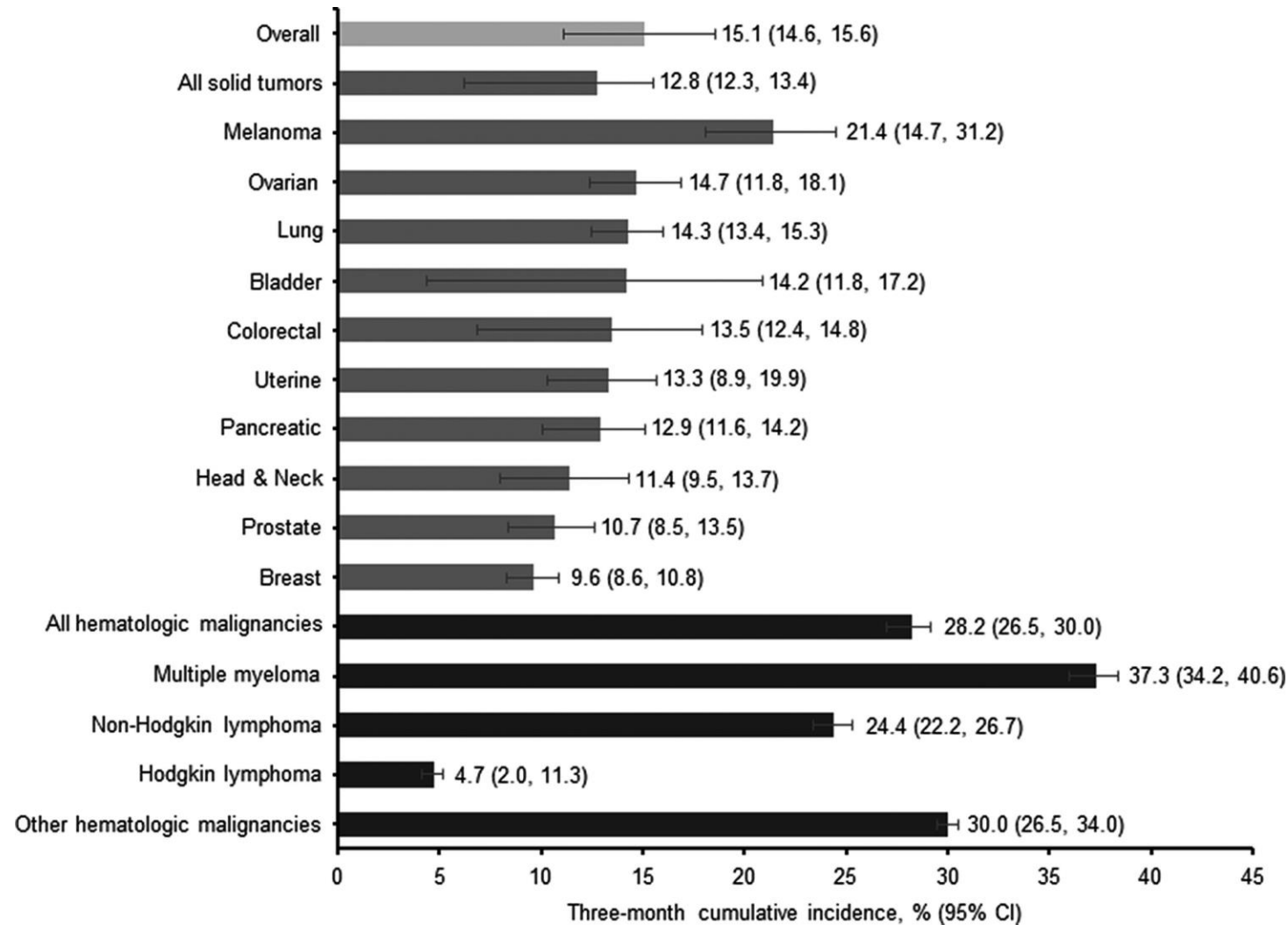
Platelet bound by autoantibodies

ITP

Meds

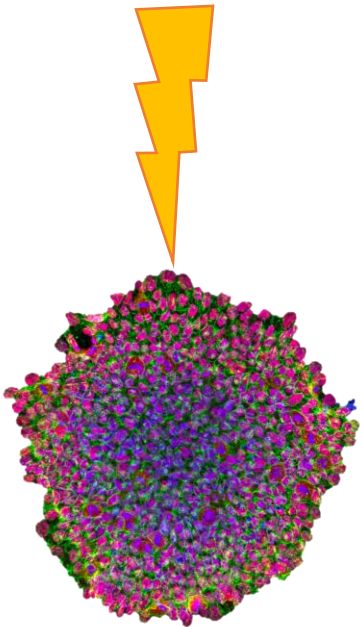


Thrombocytopenia due to Chemotherapy



CIT

Alkylating
Agents



Pluripotent
Stem Cell

Cyclophosphamide
Bortezomib



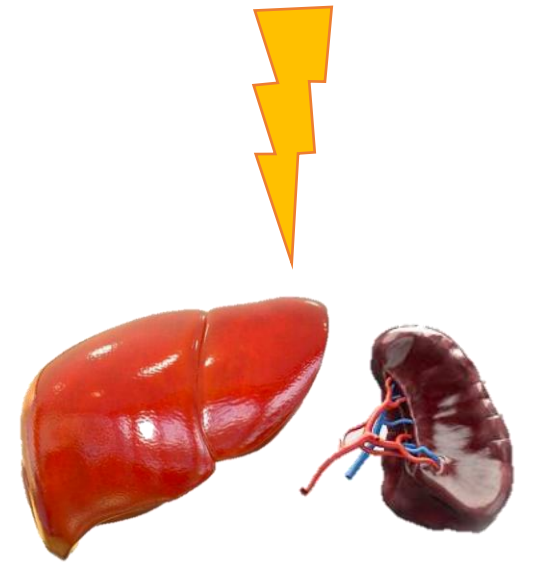
Megakaryocyte

Fludarabine



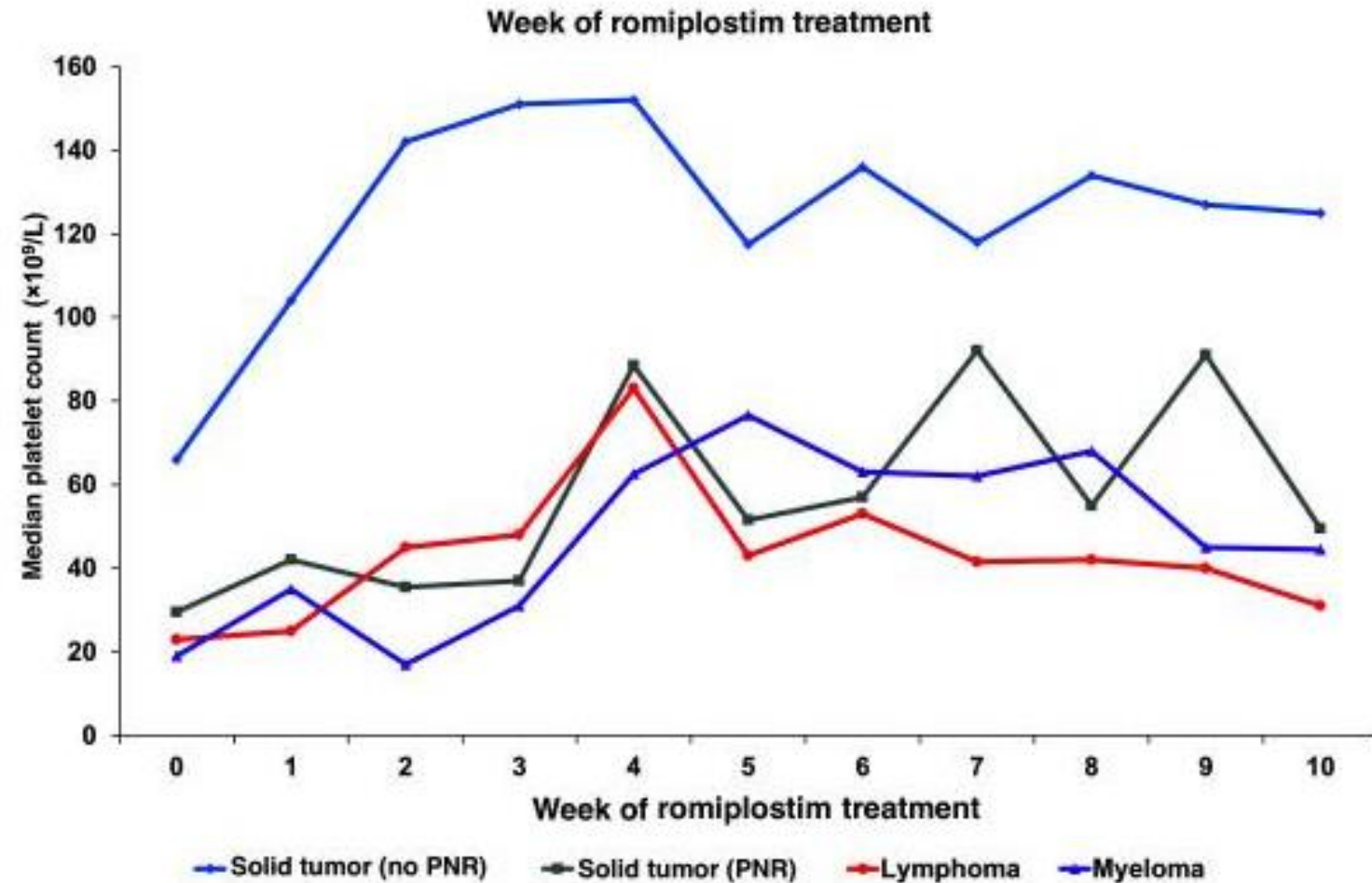
Platelet

Gemtuzumab
ozogamicin



Liver and Spleen

Treatment of CIT: Romiplostim

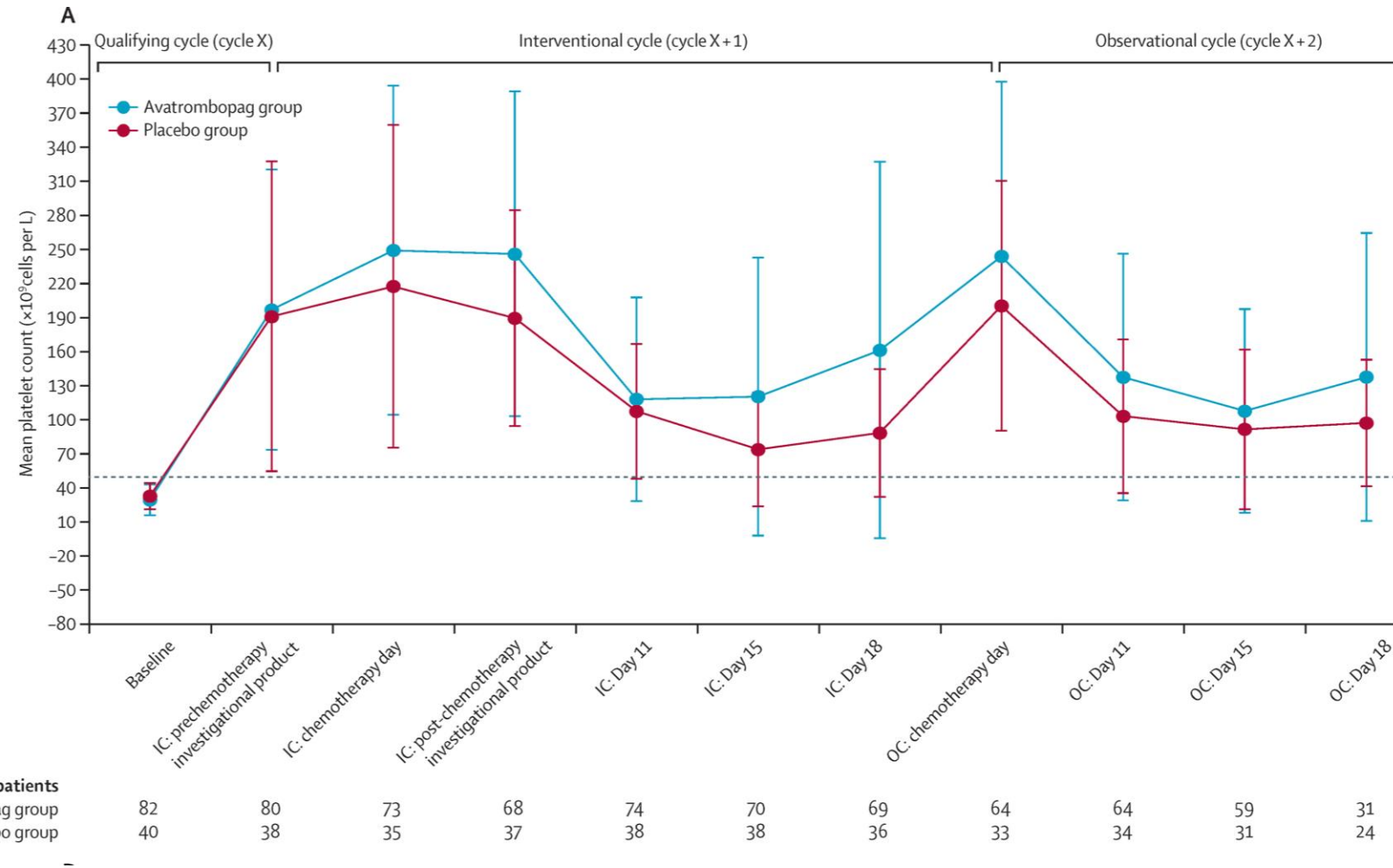


Predictors of Non-Response:

- Bone marrow invasion
- Prior pelvic radiation
- Prior temozolomide

Mean dose of romiplostim was 2.6 mcg/kg

Treatment of CIT: Avatrombopag



No significant difference in the need for chemotherapy dose reduction, treatment delay, or platelet transfusion between patients treated with avatrombopag or placebo

Case 3

- Ms. C continues to have thrombocytopenia with platelets 20-30k between cycles despite dose reduction of her chemotherapy.
 - She has occasional nose bleeds and bleed heavily from port access

Treatment of CIT



Plt <50k on 1st
day of next cycle



Mid-cycle nadir
< 20k but
recovery by
Day 1 of next
cycle



Romiplostim
2mcg/kg

- Dose weekly
- Titrate to plt
100-200k

bleeding

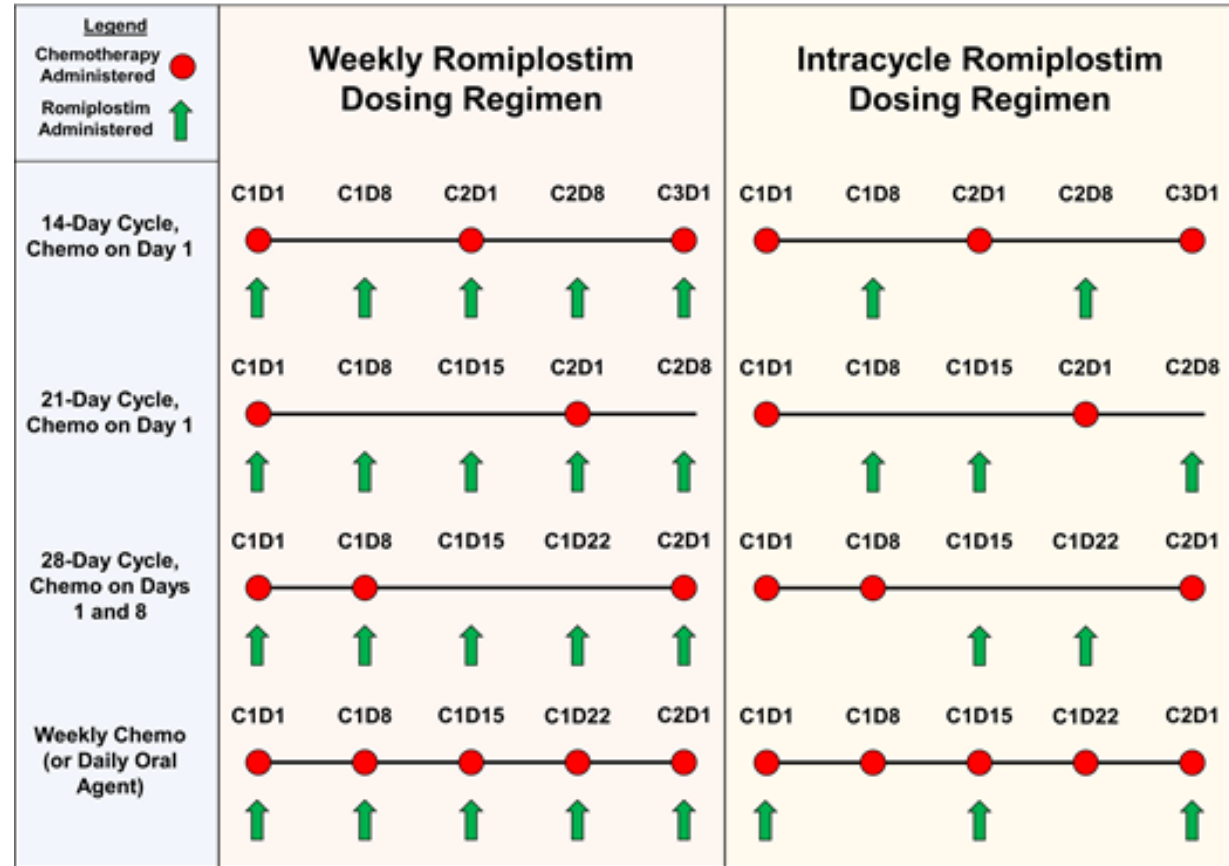
No
bleeding



Monitor as
patients unlikely
to benefit from
TPO

Case 3

- Ms C is started on weekly romiplostim 3mcg/kg with improvement in platelet counts to 50-60k reducing interruptions in her therapy



Case 4

- Ms. D 28yo primigravida F at 36 weeks gestation presents to her OB appointment with epigastric pain and is found to have hypertension and new anemia.

Case 4

- CBC

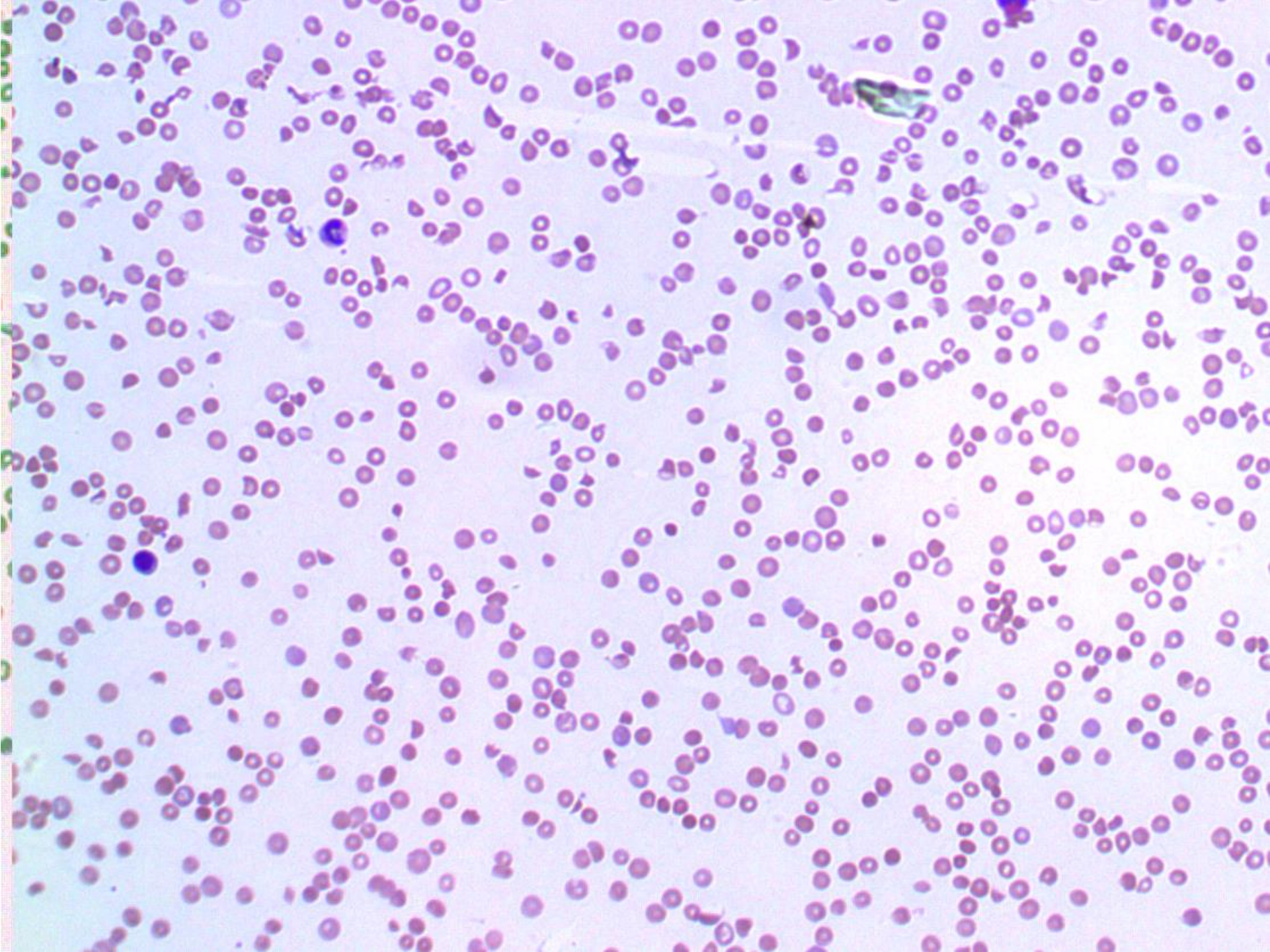
- Hgb 6.8 (L)
- Plt 33(L)

- Metabolic panel

- Cr 1.4 (H)
- AST 220 (H)
- ALT 240 (H)
- Tbili 4.8 (H)

- Coags

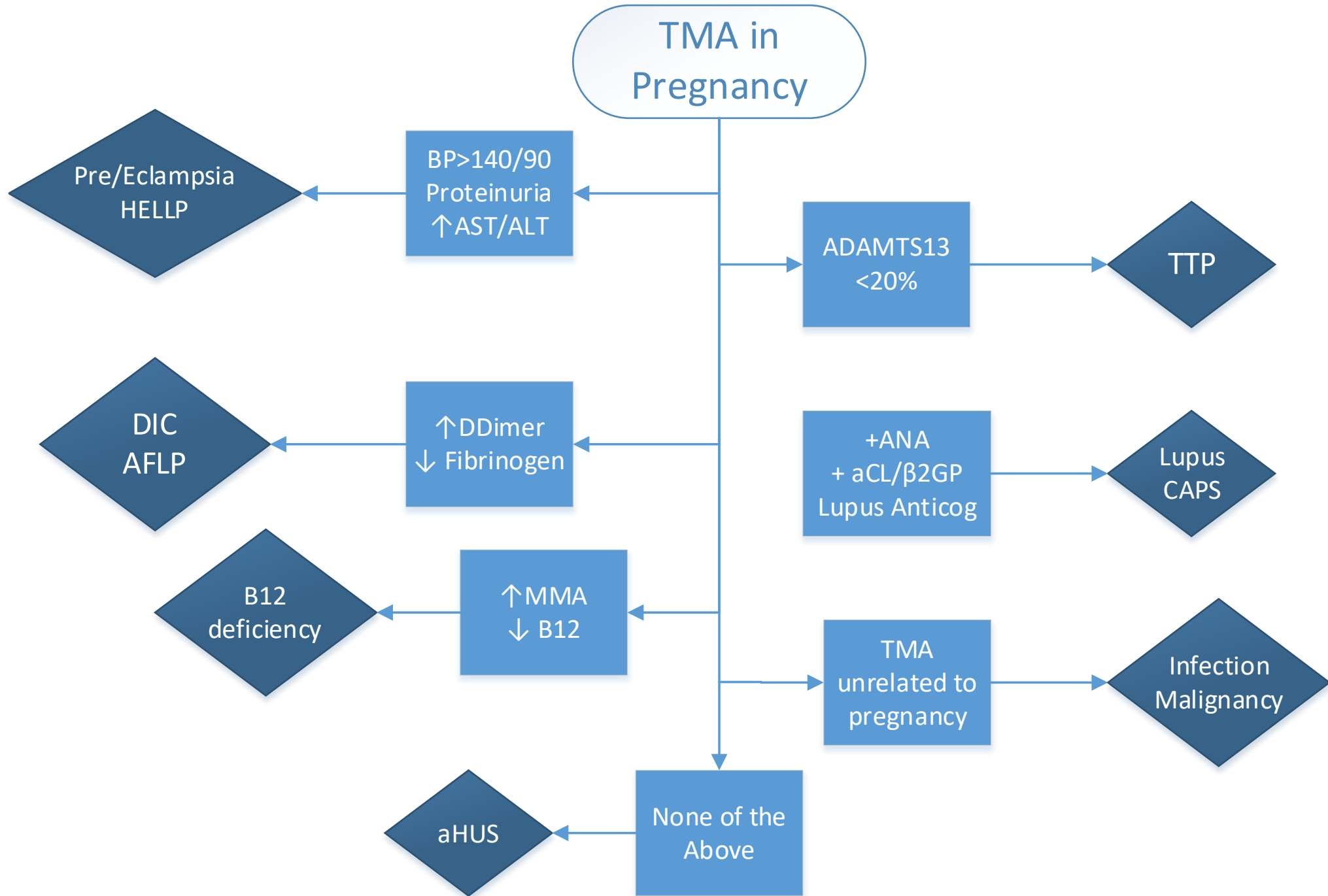
- PT 20.3 (H)
- PTT 64.4 (H)
- LDH 1200 (H)
- Hapto <8 (L)



TMA in Pregnancy

TMA in pregnancy

	HELLP	AFLP	TTP	aHUS
↓Plt	Mod/Severe	Mild/Mod	Severe	Mod/Severe
MAHA	Mod/Severe	Mild	Mod/Severe	Mod/Severe
Coag defect	Mild/Mod	Severe	None	None
HTN	Mod/Severe	Variable	Variable	Mild/absent
Liver Dys	Mod/Severe	Severe	Absent	Absent
Renal Dys	Absent-Mod	Absent-Mild	Absent-Mod	Severe
CNS Dys	Absent-Mod	Variable	Can be Severe	Absent-Mild
Trimester	Late 2 nd -3 rd	3 rd	2 nd -3 rd	Postpartum

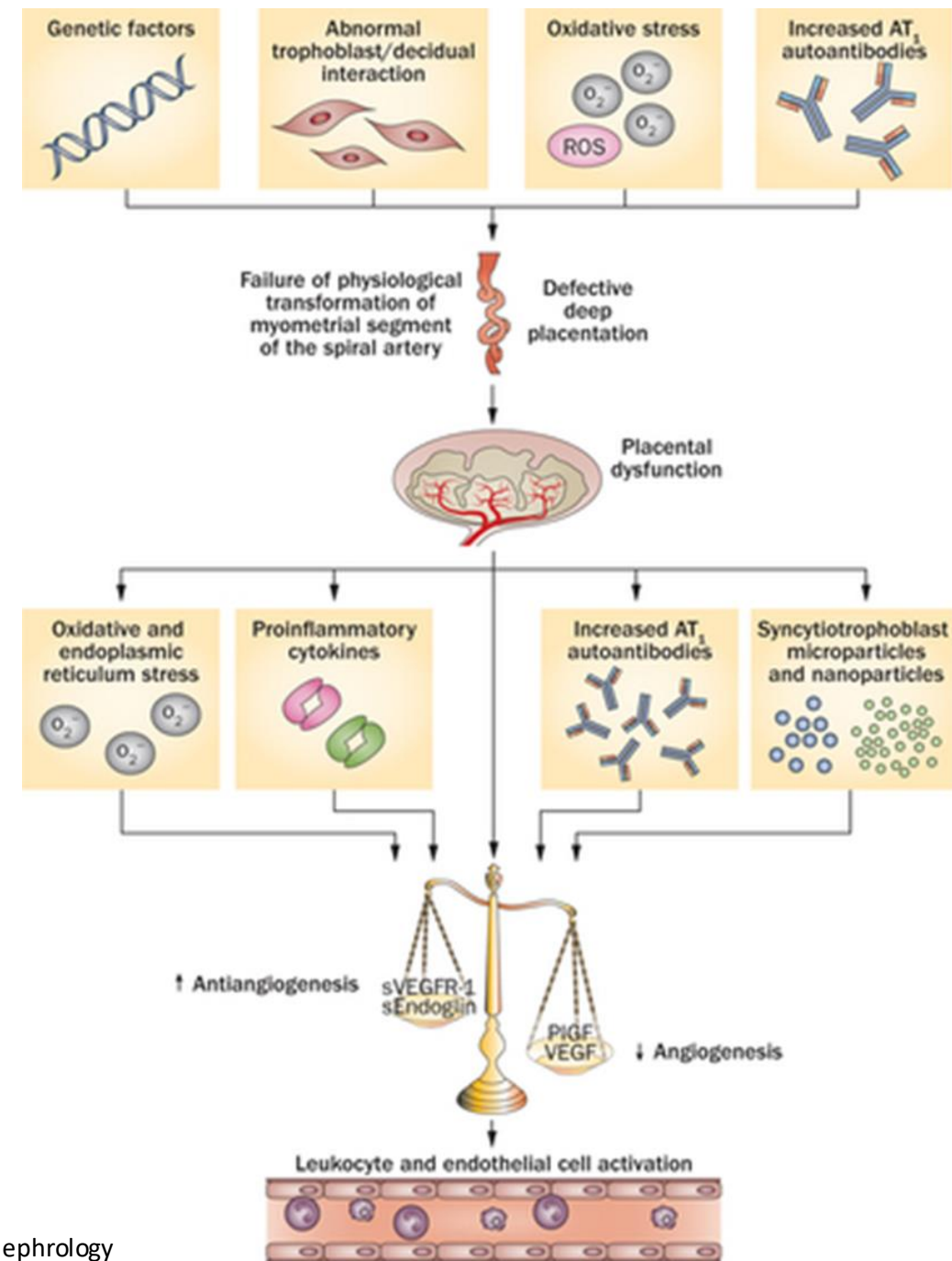


Case 4

- CBC
 - Hgb 6.8 (L)
 - Plt 33(L)
- Metabolic panel
 - Cr 1.4 (H)
 - AST 220 (H)
 - ALT 240 (H)
 - Tbili 4.8 (H)
- UA
 - 1+ blood
 - 2+ protein
- Phys Exam
 - Afebrile
 - 3+ pitting LEE
 - BP 180/110

Case 4

- Ms. D is diagnosed with HELLP
- MAHA
 - Schistocytes on smear
 - LDH > 600
- Liver Dysfunction
 - AST > 70
- Thrombocytopenia
 - Plt < 100

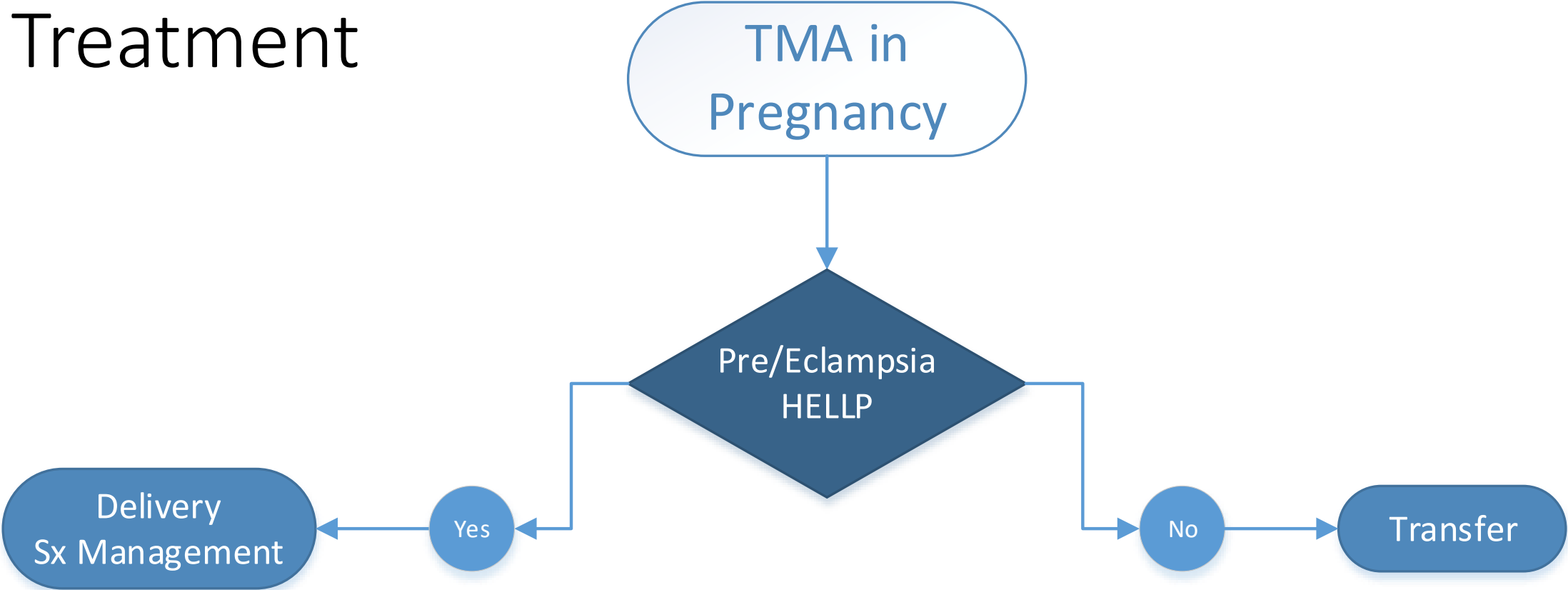


Treatment



- Delivery is the treatment of choice
 - hemodynamic instability
 - fetus >32 weeks
- Transfuse PRBCs, FFP, cryo
- Usually resolves within 48 hours after delivery
 - Steroids/PLEX if persistent symptoms 5-7 days post partum

Treatment



Thank You

