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Management of chemotherapy-induced thrombocytopenia

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Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Learning Objectives

At the end of this session, learners should be able to:

- *Recognize chemotherapy-induced thrombocytopenia (CIT) and risk factors associated with CIT*
- *Identify chemotherapies associated with CIT*
- *Outline current recommendations for the management of CIT*
- *Select a therapy plan for an example patient case dealing with CIT*

Outline

1. Background
2. Guideline Recommendations
3. Review of agents
4. Literature Review
5. Patient Case
6. Future

Abbreviation Key

AABB- American Association of Blood Banks
ALL- acute lymphoblastic leukemia
ALT- alanine aminotransferase
AML- acute myeloid leukemia
ANC- absolute neutrophil count
ASA- aspirin
ASCO- American Society of Clinical Oncology
AST- aspartate aminotransferase
AUC- area under the curve
BCRP- breast cancer resistance protein
BID- twice a day
BMI- body mass index
BP- blood pressure
BPM- beats per minute
CBC- complete blood count
CHL- Classic Hodgkin lymphoma
CIT- chemotherapy-induced thrombocytopenia
CRC- colorectal cancer
CTCAE- Common Terminology Criteria for Adverse Events
DDAbs- drug-dependent antibodies
DI- drug interaction
DIT- drug-induced thrombocytopenia
DITP- drug induced immune thrombocytopenia
DOC- drug of choice
DVT- deep venous thromboembolism
EPO- erythropoietin
G-CSF- granulocyte colony-stimulating factor
HAT- heparin associated thrombocytopenia
Hgb- hemoglobin
HIT- heparin induced thrombocytopenia
HR- heart rate
HTN- hypertension
HSC- hematopoietic stem cell
HSCT- hematopoietic stem cell transplantation
ICTMG- International Collaboration for Transfusion Medicine Guidelines
IgG- immunoglobulin G
IL- interleukin
ISTH- International Society on Thrombosis and Haemostasis
ITP- immune thrombocytopenia
IV- intravenous
LFT- liver function test
LLN- lower limit of normal
LMWH- low-molecular weight heparin
LUE- left upper extremity
MGDF- megakaryocyte growth & development factor
NCCN- National Comprehensive Cancer Network
NHL- Non-Hodgkin lymphoma
NSAIDS- nonsteroidal anti-inflammatory drugs
NSCLC- non-small-cell lung cancer
OR- odds ratio
PLT- platelet
PRBC- packed red blood cells
QID- four times a day
RBC- red blood cell
rhTPO- recombinant human thrombopoietin
RR- respiratory rate
SCr- serum creatinine
Temp- temperature
TID- three times a day
TPO- thrombopoietin
TPO-RA- thrombopoietin-receptor agonist
URTI- upper respiratory tract infection
WBC- white blood cell count
WHO- World Health Organization

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Background

Chemotherapy-induced thrombocytopenia

- **Platelets < 100 x 10^9/L**[1,2]
- ≥ 3-4 weeks following last chemotherapy administration[1]
- Time to thrombocytopenia varies[3]:
  - ~5 weeks in platinum-based regimens for breast cancer and NHL
  - ~3 weeks in platinum-based regimens in CRC and ovarian cancer
  - Shorter time to thrombocytopenia in older vs younger patients

Grading thrombocytopenia- CTCAE v6.0[4]

Grade	Criteria
Grade 1	< LLN- 75.0 x 10^9/L
Grade 2	< 75.0- 50.0 x 10^9/L
Grade 3	< 50.0- 10.0 x 10^9/L; transfusion indicated
Grade 4	< 10.0 x 10^9/L; life-threatening consequences; urgent intervention indicated
Grade 5	Death

CIT vs other thrombocytopenias

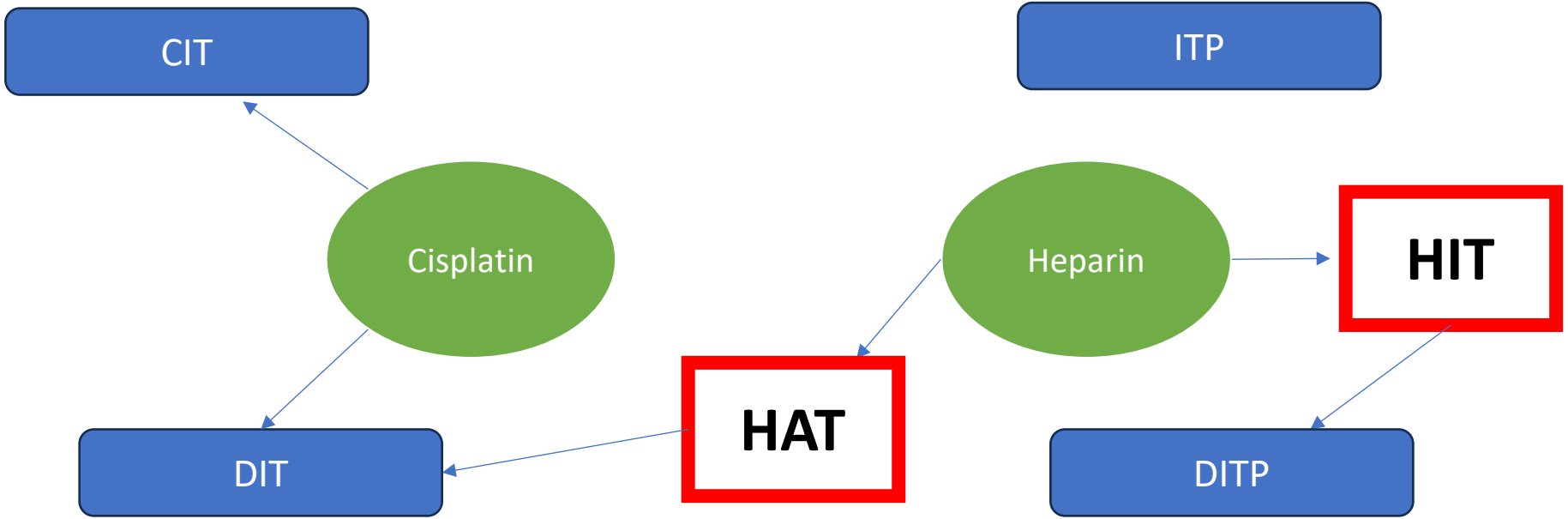
- **Drug-induced thrombocytopenia (DIT)**[5]
  - Nonimmune
  - Direct cytotoxic effect on megakaryocytes and/or platelets
  - Dysfunctional thrombopoiesis within bone marrow or increased platelet destruction (proapoptotic effect)

- **Immune thrombocytopenia (ITP)**[6]
  - Immunoglobulin G (IgG) autoantibodies sensitizing circulating platelets

- **Drug-induced immune thrombocytopenia (DITP)**[5]
  - Drug-dependent antibodies (DDAbs)
  - Platelets targeted only in the presence of the sensitizing drug

CIT vs other thrombocytopenias

CIT vs other thrombocytopenias



Assessment Question #1

Which one of the following would be considered CIT?

a. Plt 80 x 10^9/L following heparin administration in a patient in remission
b. Plt 150 x 10^9/L in a patient with ALL after receiving C2D2 of cyclophosphamide and etoposide
c. Plt 30 x 10^9/L in a patient with multiple myeloma presenting with a GI bleed
d. Plt 45 x 10^9/L in a patient with ovarian cancer after receiving C2D1 of cisplatin and gemcitabine

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d. Plt 45 x 10^9/L in a patient with ovarian cancer after receiving C2D1 of cisplatin and gemcitabine

Why do we care about CIT?

Plt < 100 x 10^9/L	Plt < 50 x 10^9/L	Plt < 10 x 10^9/L
• Caution administering chemo/radiation due to risk of bleeding & worsening thrombocytopenia[2]	• Surgical procedures complicated by bleeding[2]	• Risk of spontaneous bleeding is increased[2]

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Why do we care about CIT?

Therapeutic delays[7]

Chemo dose and frequency reductions[2,7]

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Risk Factors for CIT

- Non-chemo drugs with baseline thrombocytopenic risk
- Type of cancer
- Class of chemotherapy

Non-chemo drugs

Antibiotics[5]	Linezolid, vancomycin
Thiazide diuretics[5]	Chlorothiazide, hydrochlorothiazide, metolazone
Drugs with "platelet activity"	NSAIDS, ASA, heparin, LMWH, P2Y12 inhibitors, glycoprotein IIb/IIIa inhibitors
Other agents[5]	Ganciclovir, lovastatin

Cancer type

- One-third of patients with a solid tumor diagnosis[7]
  - Highest prevalence in colorectal cancer, followed by NSCLC and ovarian cancer[3]
- 50-68% of patients with a hematologic malignancy[3,7]

Class of chemo

- Chemotherapy agents differ in how they cause thrombocytopenia[2]
  - Alkylating agents act on stem cells
  - Cyclophosphamide affects later megakaryocyte progenitors
  - Bortezomib prevents platelet release from megakaryocytes
  - Other treatments promote platelet apoptosis
- Highest risk of CIT[3]
  - Gemcitabine-based regimens
  - Platinum-based regimens

Frequencies of thrombocytopenia with selected chemo regimens[2]

Regimen	Cancer	Thrombocytopenia	
		Grade 3	Grade 4
Ibritumomab tiuxetan (n=30)	NHL	~87%	13%
Bortezomib (n=193)	Myeloma	28%	3%
Carboplatin (n=55)	Various cancer types	23%	
ICE (n=16)	NHL	-	35%
Gemcitabine [1 g/m2 (D1 & 8)] & cisplatin [60 mg/m2 (D1)]; q 3 weeks (n=26)	Pancreas	2.8%	
Gemcitabine [1.25 g/m2 (D1 & 8)] & cisplatin [75 mg/m2 (D1)]; q 3 weeks (n=830)	NSCLC	13%	
Gemcitabine [1 g/m2 (D1 & 8)] & carboplatin [AUC=5 (D1)]; q 3 weeks (n=217)	NSCLC	32%	24%

Assessment Question #2

70 year-old male with CHL (hematologic malignancy), on GEMOX (gemcitabine/oxaliplatin) is started on enoxaparin for DVT prophylaxis following admission to the medical oncology floor.

How many risk factors for CIT does this patient have?

a. 2

b. 3

c. 4

d. 5

Assessment Question #2

70 year-old male with CHL (**hematologic malignancy**), on GEMOX (**gemcitabine/oxaliplatin**) is started on **enoxaparin** for DVT prophylaxis following admission to the medical oncology floor.

How many risk factors does this patient have?

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b. 3

c. 4

d. 5

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Guideline Recommendations

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2024 NCCN Guidelines for Hematopoietic Growth Factors

- **Evaluate for other potential causes of thrombocytopenia**
  - CBC w/differential
  - Rule out nutritional deficiencies, infection, medications that suppress platelet production, ITP, HIT, radiation or chemotherapy induced myelosuppression, bone marrow involvement by underlying malignancy, etc.

- **Transfuse if Plt < 10 x 10^9/L** [strong recommendation, moderate-certainty of evidence] per the 2025 AABB/ICTMG Platelet Transfusion Guidelines[8]
  - Non-bleeding patients
  - Chemo or undergoing allogeneic stem cell transplant

2024 NCCN Guidelines for Hematopoietic Growth Factors

Clinical trial enrollment recommended for use of TPO-RAs

Chemotherapy dose reduction or change in treatment regimen

2024 NCCN Guidelines for Hematopoietic Growth Factors

Clinical trial enrollment recommended for use of TPO-RAs

Chemotherapy dose reduction or change in treatment regimen

2024 NCCN Guidelines for Hematopoietic Growth Factors

- **Romiplostim: TPO-RA of choice**
  - **Purpose:** Maintain dose schedule and intensity of chemo
  - **Dose:** Weekly, beginning at 2-4 mcg/kg, increased no more than 1-2 mcg/kg/week
  - **Target platelet count: 100-150 x 10^9/L**
  - **Max dose:** 10 mcg/kg weekly
  - Insufficient data for routine use in pediatric patients

2024 ISTH CIT Guidelines[7]

- **Transfuse if platelets < 10 x 10^9/L**
- Transfuse if serious bleeding (WHO grade ≥ 2) and less severe thrombocytopenia (< 50 x 10^9/L)
- **Do not transfuse prophylactically to allow for full-dose chemotherapy**
- **Recommend enrollment in clinical trial for TPO-RAs**
  - May consider use of TPO-RA to avoid dose reduction or delay ≥ 7 days
  - **DOC: Romiplostim**

2024 ISTH CIT Guidelines

- Recommend **against** the use of TPO-RAs outside of a clinical trial if:
  - AML or high-risk myelodysplasia
  - HSCT
  - Lymphoma

- **Target platelet count: 100-200 x10^9/L**

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Thrombopoietin Receptor Agonists (TPO-RAs)

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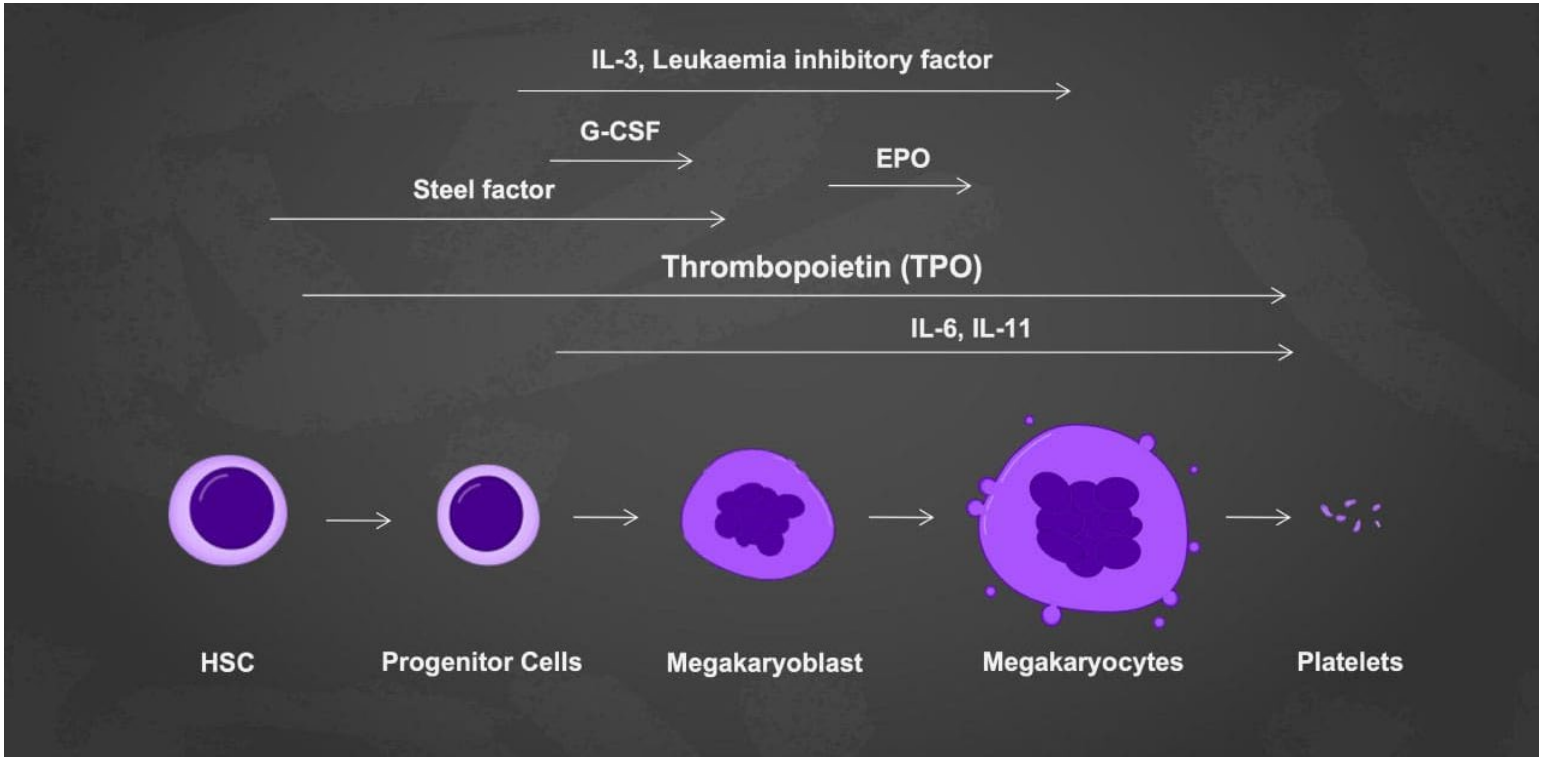
Life cycle of a platelet



My Hematology. Published December 17, 2023. https://myhematology.com/platelet-disorders/platelets-guardians-of-hemostasis/

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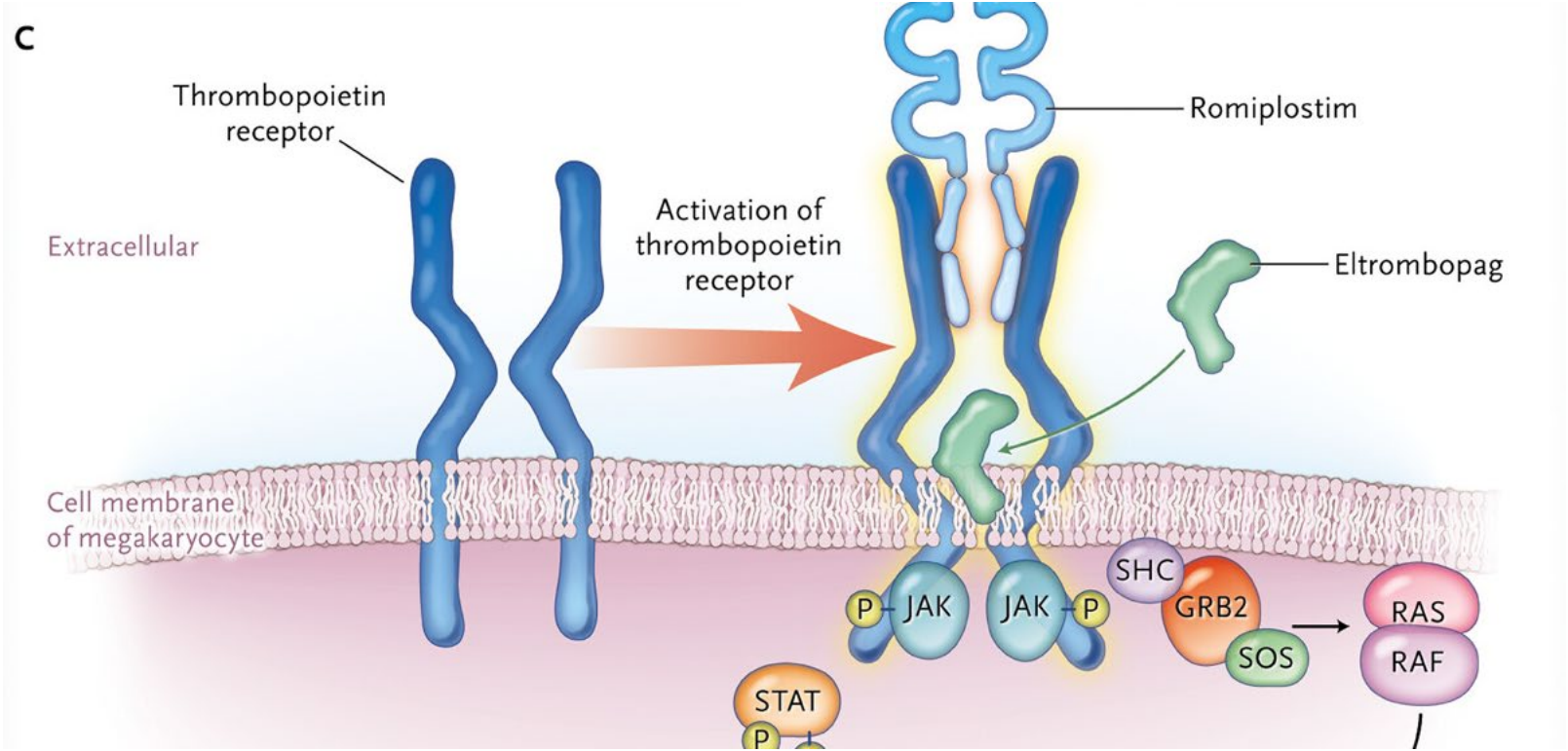
Mechanism of action



N Engl J Med. 2011;365(8):734-741. doi:10.1056/NEJMct1014202

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	Romiplostim	Lusutrombopag	Eltrombopag	Avatrombopag
Indication	ITP in adults and children >1 year old	Thrombocytopenia in adult patients with chronic liver disease who are schedule to undergo a procedure	Chronic ITP in adults and children >1 year old; chronic hepatitis C patients whose thrombocytopenia limits ability to maintain interferon-based therapy; severe aplastic anemia	Chronic ITP; patients with chronic liver disease who are scheduled to undergo a procedure
Route of administration	Subcutaneous	Oral	Oral	Oral
Administration instructions	Prepared and injected by a health care professional once weekly	Take once daily with or without food	Take once daily without food or with a meal < 50 mg of calcium, separate from products with polyvalent cations, do not crush	Take with food, tablets may be crushed and mixed with yogurt or pudding

Drugs. 2021;81(11):1285-1305. doi:10.1007/s40265-021-01553-7

	Romiplostim	Lusutrombopag	Eltrombopag	Avatrombopag
Monitoring	• CBC weekly, then monthly once stable dose achieved • Once discontinued, CBC weekly for at least 2 weeks	• CBC at baseline and within 2 days prior to scheduled procedure	• LFTs at baseline and every 2 weeks, then monthly after stable dose achieved • CBC • Baseline ocular examination • DI with polyvalent cations, OATP1B1, and BCRP substrates	• CBC weekly until stable Plt > 50 x 10^9/L, then monthly • Once discontinued, CBC weekly for at least 4 weeks • DI with CYP2C9 and CYP3A4 inducers/inhibitors
AWP (USD)	$1238.82/125-µg vial	$1457.14/3 mg tab	$225.61-612.43/tab (12.5, 25, 50, and 75 mg)	$391.68/20 mg tab

Drugs. 2021;81(11):1285-1305. doi:10.1007/s40265-021-01553-7

TPO-RA Adverse Events[9]

- All TPO-RA
  - Headache
  - Fatigue
- Avatrombopag
  - Epistaxis
  - URTI
- Eltrombopag
  - Increase in ALT/AST & blood bilirubin
  - Cataract
- Romiplostim
  - Arthralgia
  - Myalgia
  - Insomnia

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Literature Review

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Systematic literature review and meta-analysis on use of Thrombopoietic agents for chemotherapy-induced thrombocytopenia[10]

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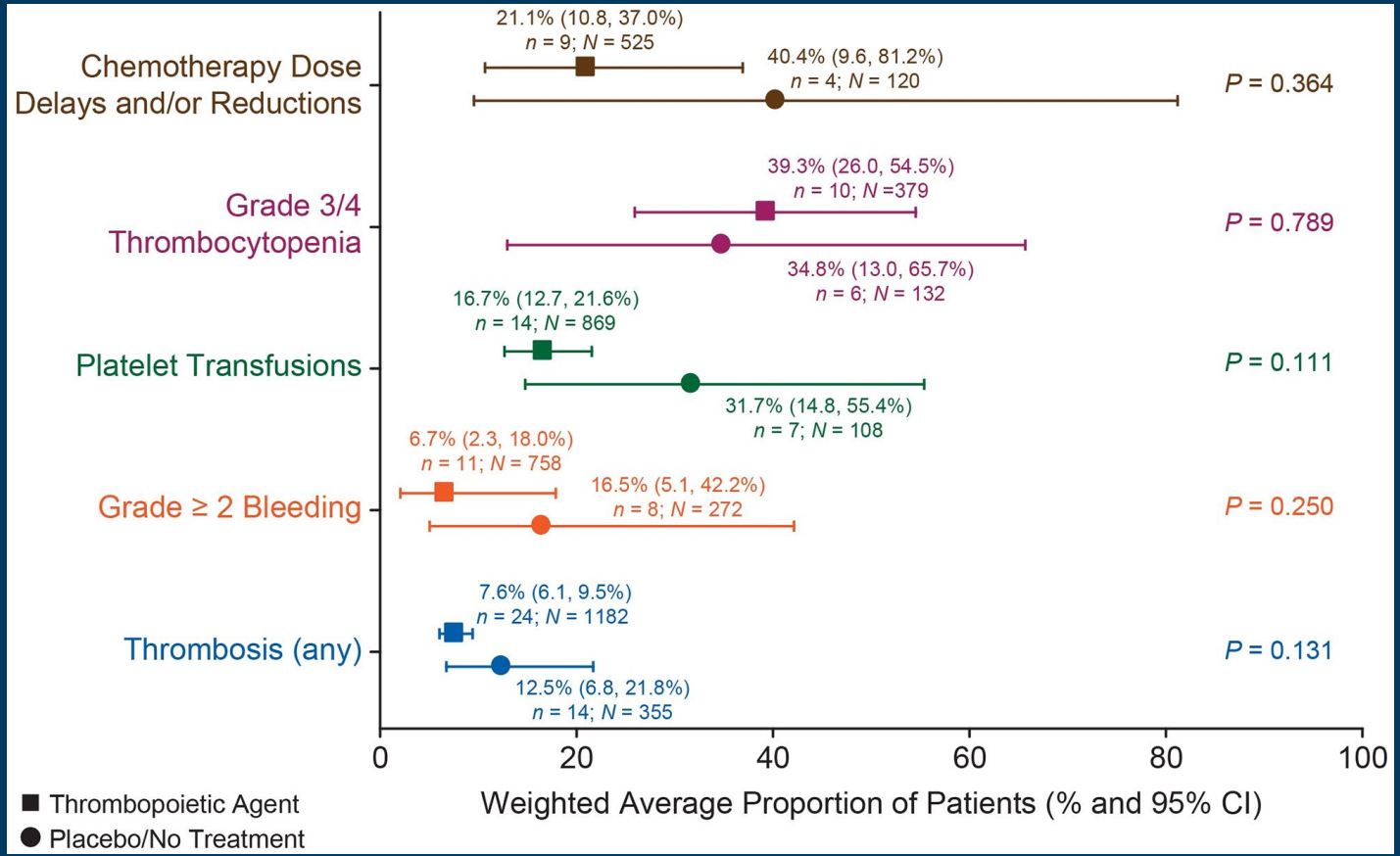
Background

- **Objective:** Evaluate the efficacy and safety of the use of thrombopoietic agents in patients with CIT compared to placebo or standard-of-care treatments (chemotherapy dose delays and/or reductions and platelet transfusions)

- **Study design and methodology:**
  - 34 clinical trials & 5 observational studies (n=39) from January 1995-March 2021
  - Accepted interventions: rhTPO, MGDF, romiplostim, eltrombopag, avatrombopag, lusutrombopag
  - Excluded studies with n < 20 and non-English language studies

Endpoints of interest

1. Time to first platelet recovery
2. Incidence of chemotherapy dose delay by ≥ 4 days
3. Incidence of chemotherapy dose reduction of ≥ 15% due to platelet counts < 100 x 10^9/L
4. Incidence of platelet transfusions
5. Incidence of grade ≥ 2 bleeding



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Results

- Study population mostly hematopoietic malignancies and NSCLC on platinum-based treatments or cytarabine
- Thrombopoietic agents did not significantly decrease dose delays and/or reductions compared with placebo/no treatment, or any of the other endpoints of interest
- General benefit of thrombopoietic agents can be seen among individual studies
  - Significantly improve platelet counts

Takeaways

- rhTPO and MGDF?
- Only 3/34 clinical trials included were considered to have a low risk of bias (Cochrane's Risk of Bias)
- Dosing and dosing schedules for all thrombopoietic agents were inconsistent across studies
- My meta-analysis:
  - Include mortality as an end-point
  - Exclude hemopoietic malignancies
  - Only assess TPO-RAs

Patient Case

Patient Case

IN is a 62-year-old female with stage 3C ovarian cancer with metastases to intestines on C1D21 of liposomal doxorubicin 30 mg/m^2 and carboplatin (AUC=5).

She presents with worsening abdominal pain, nausea, fatigue, and decreased appetite.

In 8 days, she is scheduled for her second cycle of doxorubicin and carboplatin.

Patient Case

PMH	Vitals	Pertinent labs	Medications
• Cholecystectomy • Ileostomy • LUE DVT • HTN	• Temp: 36.2°C • HR: 79 bpm • RR: 16 bpm • BP: 108/72 mmHg • BMI: 19.21 kg/m^2	• WBC: 7.4 • RBC: 3.33 • Hgb: 10.4 • **Plt: 46 K/mcL** • ANC: 4.3 • AST/ALT: 38/46 units/L • Albumin: 2.7 g/dL • SCr: 0.75	• Diphenoxylate-atropine 5-0.05 mg BID • Eliquis 5 mg BID • Gabapentin 300 mg Q8H • Magnesium oxide 400 mg TID • Metoclopramide 10 mg QID

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Assessment Question #3

Medications
• Carboplatin 350 mg IV • Diphenoxylate-atropine 5-0.05 mg BID • Doxorubicin liposomal 44 mg IV • Apixaban 5 mg BID • Gabapentin 300 mg Q8H • Magnesium oxide 400 mg TID • Metoclopramide 10 mg QID

Which of the following agents is most likely causing this patient's thrombocytopenia?

a. Metoclopramide

b. Diphenoxylate-atropine

c. Carboplatin

d. Apixaban

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Assessment Question #3

Medications

- Carboplatin 350 mg IV
- Diphenoxylate-atropine 5-0.05 mg BID
- Doxorubicin liposomal 44 mg IV
- Apixaban 5 mg BID
- Gabapentin 300 mg Q8H
- Magnesium oxide 400 mg TID
- Metoclopramide 10 mg QID

Which of the following agents is most likely causing this patient's thrombocytopenia?

a. Metoclopramide

b. Diphenoxylate-atropine

c. Carboplatin

d. Apixaban

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Assessment Question #4

Which of the following would you recommend to manage this patient's CIT?

a. Transfuse with 1 unit of PRBC

b. Hold apixaban

c. Initiate romiplostim; enroll in clinical trial if able

d. Initiate high-dose steroids

Assessment Question #4

Which of the following would you recommend to manage this patient's CIT?

a. Transfuse with 1 unit of PRBC

b. Hold apixaban

c. Initiate romiplostim; enroll in clinical trial if able

d. Initiate high-dose steroids

Assessment Question #5

7 days after receiving romiplostim, platelets are now **40 x 10^9/L**. Tomorrow, the patient is scheduled to start Cycle 2 of doxorubicin/carboplatin. What would you recommend as the next step in managing this patient's CIT?

a. Enroll in a different TPO-RA clinical trial

b. Transfuse with 1 unit of PRBC

c. Discontinue current chemotherapy regimen and initiate a different regimen

d. Delay chemotherapy; allow for platelet count to recover

Assessment Question #5

7 days after receiving romiplostim, platelets are now **40 x 10^9/L**. Tomorrow, the patient is scheduled to start Cycle 2 of doxorubicin/carboplatin. What would you recommend as the next step in managing this patient's CIT?

a. Enroll in a different TPO-RA clinical trial

b. Transfuse with 1 unit of PRBC

c. Discontinue current chemotherapy regimen and initiate a different regimen

d. Delay chemotherapy; allow for platelet count to recover

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Future of CIT management

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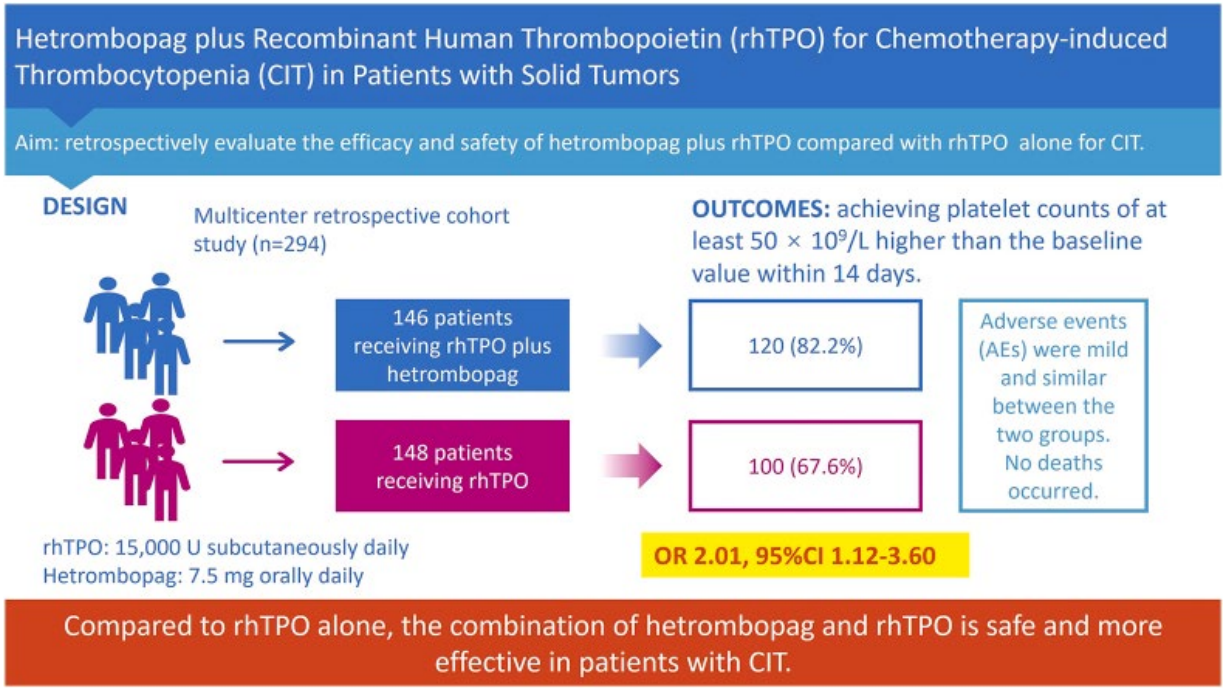
Promising future for CIT research

- 215 NSCLC patients treated with gemcitabine/carboplatin were whole-exome sequenced to identify genetic markers associated with CIT[11]
  - Researchers were able to identify and validate genetic variations within hematopoiesis-related pathways

- RECITE phase 3 trial (Al-Samkari, et al.)
  - 165 colorectal, gastroesophageal, or pancreatic cancer patients receiving oxaliplatin-based regimens
  - Romiplostim vs placebo for **Plt ≤ 85 x 10^9/L**
  - Primary endpoint: No CIT-induced dose modification
  - Presented at 2025 ASCO conference

Promising future for CIT research



Res Pract Thromb Haemost. 2023;7(7):102231. doi:10.1016/j.rpth.2023.102231

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Current clinical trials for TPO-RAs

- **PROCLAIM trial (phase 3, NCT03937154): Romiplostim for CIT in NSCLC, ovarian, or breast cancer**
- Romiplostim to prevent CIT in patients >1 year old with Ewing Sarcoma (single-arm study, NCT07048249)
- ACT-GI trial (phase 2, NCT05772546): Avatrombopag for CIT in GI malignancies

Summary/Conclusion

- Current guidelines recommend against the use transfusions prophylactically and **only if Plt 10 x 10^9/L**
- TPO-RAs are recommended if their use will allow for full-dose administration of chemotherapy and prevent delays
- There are currently **no FDA-approved TPO-RAs for CIT**
- What patients still need:
  - High-quality studies, long-term follow-up
  - Morbidity/mortality
  - Clinical trials

References

1.Hematopoietic Growth Factors. NCCN clinical practice guidelines in oncology (NCCN Guidelines®); 2023. https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf

2. Kuter DJ. Managing thrombocytopenia associated with cancer chemotherapy. Oncology (Williston Park). 2015;29(4):282-294.

3. Shaw JL, Nielson CM, Park JK, Marongiu A, Soff GA. The incidence of thrombocytopenia in adult patients receiving chemotherapy for solid tumors or hematologic malignancies. Eur J Haematol. 2021;106(5):662-672. doi:10.1111/ejh.13595

4. Common Terminology Criteria for Adverse Events (CTCAE) Version 6.0 [Excel file]. Bethesda, MD: National Cancer Institute; 2025. Accessed September 3, 2025.

5. Bakchoul T, Marini I. Drug-associated thrombocytopenia. Hematology Am Soc Hematol Educ Program. 2018;2018(1):576-583. doi:10.1182/asheducation-2018.1.576

6. Pietras NM, Gupta N, Justiz Vaillant AA, Pearson-Shaver AL. Immune Thrombocytopenia. In: StatPearls. Treasure Island (FL): StatPearls Publishing; May 5, 2024.

7. Soff G, Leader A, Al-Samkari H, et al. Management of chemotherapy-induced thrombocytopenia: guidance from the ISTH Subcommittee on Hemostasis and Malignancy. J Thromb Haemost. 2024;22(1):53-60. doi:10.1016/j.jtha.2023.09.031

8. Metcalf RA, Nahirniak S, Guyatt G, et al. Platelet Transfusion: 2025 AABB and ICTMG International Clinical Practice Guidelines. *JAMA*. 2025;334(7):606-617. doi:10.1001/jama.2025.7529

9. Gilreath J, Lo M, Bubalo J. Thrombopoietin Receptor Agonists (TPO-RAs): Drug Class Considerations for Pharmacists. Drugs. 2021;81(11):1285-1305. doi:10.1007/s40265-021-01553-7

10. Soff GA, Ray-Coquard I, Rivera LJM, et al. Systematic literature review and meta-analysis on use of Thrombopoietic agents for chemotherapy-induced thrombocytopenia. PLoS One. 2022;17(6):e0257673. Published 2022 Jun 9. doi:10.1371/journal.pone.0257673

11. Björn N, Sigurgeirsson B, Svedberg A, et al. Genes and variants in hematopoiesis-related pathways are associated with gemcitabine/carboplatin-induced thrombocytopenia. Pharmacogenomics J. 2020;20(2):179-191. doi:10.1038/s41397-019-0099-8

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Questions?

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