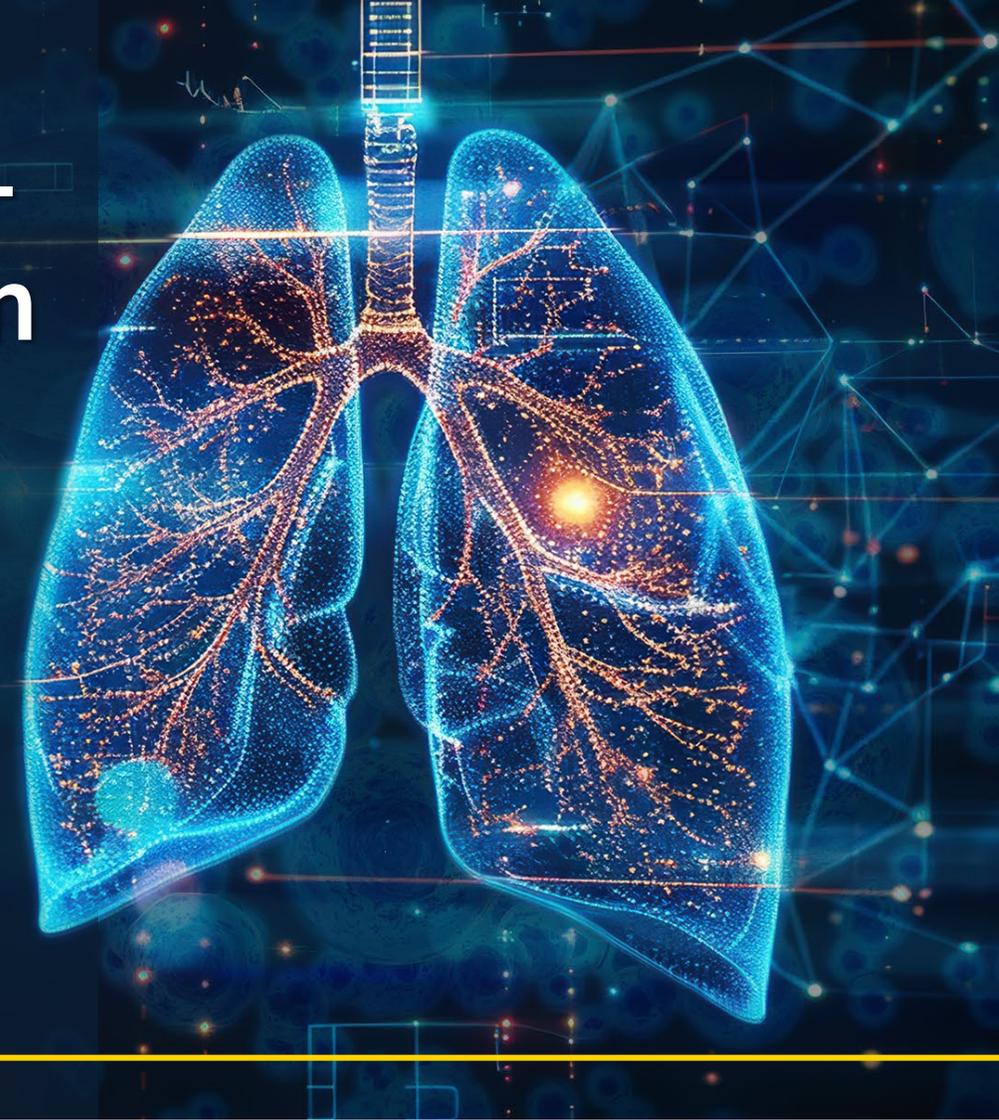


Mitigating Chemotherapy-Induced Myelosuppression in ES-SCLC:



An Expert Roadmap
for Optimizing
Clinical and Patient-
Reported Outcomes



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Faculty Disclosures

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- **Speaking Services:** Amgen, AstraZeneca, BeOne Oncology, Boehringer Ingelheim, Blueprint Medicines, BMS, Caris LifeSciences, Daiichi Sankyo, Eli Lilly, EMD Serono, Epizyme, Foundation Medicine, G1 Therapeutics, Genentech, Gilead, Janssen, Mirati Therapeutics, Myriad, Novartis, Pfizer, Puma, Regeneron, Sanofi/Genzyme, Stemline Oncology, Takeda
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- Review the prevalence, diagnostic distinctions, and dire clinical gravity of extensive-stage small cell lung cancer (ES-SCLC).
- Examine current expert consensus guideline recommendations for managing ES-SCLC, highlighting the preeminence of chemotherapy-based treatment regimens.
- Evaluate the clinical trial evidence for myeloprotective therapeutic approaches in ES-SCLC, with emphasis on the paradigm-shifting potential of multilineage myeloprotection.
- Differentiate the pharmacologic mechanism and clinical utility of CDK4/6 inhibition relative to reactive, single-lineage therapeutic approaches (i.e., G-CSF, ESAs, RBC/platelet transfusions).
- Summarize current guideline-recommended and FDA-approved supportive care strategies for protecting hematopoietic stem and progenitor cells (HSPCs) in patients being treated for ES-SCLC.

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A Closer Look at Chemotherapy-Induced Myelosuppression in ES-SCLC

Epidemiology, Patient Burden, and the Clinical Management Imperative

Chemotherapy-Induced Myelosuppression (CIM)



- May result from impairment of hematopoietic stem and progenitor cells (HSPCs) in bone marrow (BM)
- Represents a major dose-limiting and potentially life-threatening complication of chemotherapy, possibly causing dose delays/reductions and may compromise long-term clinical outcomes
- Increases morbidity and mortality
 - Higher risk of infections, bleeding complications
 - Long-term BM toxicity can result in myelodysplastic syndrome (MDS), acute leukemias, and BM exhaustion
- Affects patient safety, quality of life, and cost to the health care system

Kurtin S. *J Adv Pract Oncol.* 2012; Povsic M, et al. *PLoS One.* 2019; Epstein R, et al. *Adv Ther.* 2020; Crawford J, et al. *Support Care Cancer.* 2020; Mountzios G, et al. *Mol Clin Oncol.* 2016; Goldschmidt J, et al. *Future Oncol.* 2022; Epstein R, et al. *J Med Econ.* 2022; Hart L, et al. *Cancer Med.* 2023.



Burden of Chemotherapy-Induced Myelosuppression on Patients With Cancer

- The burden on patients (and their caregivers) is both physical and financial.
- Concerns over developing an infection and other potentially fatal complications may have a negative impact on a patient's QOL.
- It may affect the decision to continue chemotherapy.
- CIM typically requires dose delays, reductions, or discontinuations of the chemotherapy regimen.
- Potentially, it might result in suboptimal treatment outcomes.

Cytopenia	Patient Burden
Neutropenia and FN	<ul style="list-style-type: none">• Chemotherapy dose reductions and treatment delays• Increased fatigue; reduced physical, functional and emotional well-being• Increased worry about risk of infection; reduced social/family well-being• Hospitalization and increased risk of mortality (FN)• Time and financial burdens associated with hospitalizations and/or additional visits to the clinic for G-CSF administration
Anemia	<ul style="list-style-type: none">• Increased fatigue; reduced physical, functional and emotional wellbeing• Chemotherapy dose reductions and treatment delays• Time and financial burdens associated with RBC transfusion visits
Thrombocytopenia	<ul style="list-style-type: none">• Chemotherapy dose reductions and treatment delays• Risk of severe bleeding• Anxiety and fear associated with bleeding/bruising risk and dose reductions/delays• Risk of transfusion reactions and infections with platelet transfusions

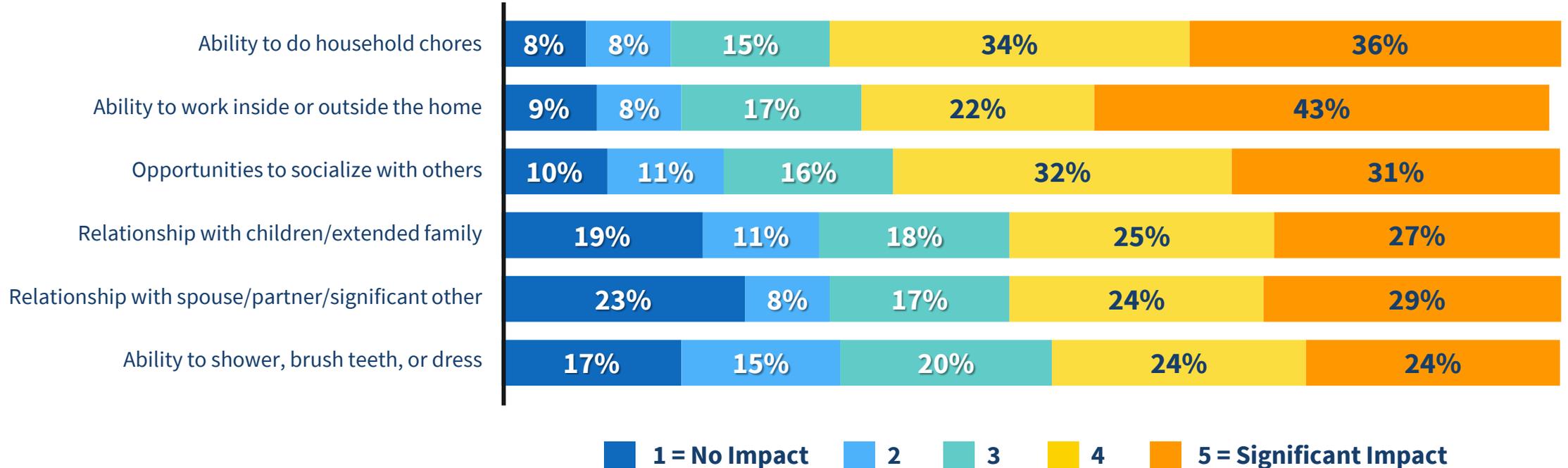
FN=Febrile neutropenia; G-CSF=granulocyte colony-stimulating factors.

Goldschmidt J, et al. *Future Oncol.* 2022; Epstein R, et al. *J Med Econ.* 2022; Crawford J, et al. *Future Oncol.* 2024; Hart L, et al. *Cancer Med.* 2023.



Real-World Impact of Chemotherapy-Induced Myelosuppression

- Participants rated a variety of aspects of daily living on a scale of 1 to 5
- 24% to 43% of participants believed that CIM and its symptoms had a significant impact on their daily lives



Goldschmidt J, et al. *Future Oncol.* 2022; Epstein R, et al. *J Med Econ.* 2022; Hart L, et al. *Cancer Med.* 2023; Epstein R, et al. *Adv Ther.* 2020; Epstein R, et al. *Patient Prefer Adherence.* 2021.



Economic Burden of Chemotherapy-Induced Myelosuppression

- Adverse-event related costs due to CIM (i.e., anemia, thrombocytopenia, and neutropenia) can burden the health care system

Direct Costs

Procedures

Tests

Devices

Drugs

Indirect Morbidity and Mortality Costs

Costs associated with patient and caregiver work loss

Time spent away from the workplace resulting from early mortality

Premature retirement

Pay for caregivers and/or non-revenue generating support centers

Decreased productivity while at work

Worker replacement

^aExpenditures for services associated with treatment and care.

^bExpenses incurred from the cessation or reduction of work and valued from either a societal, individual, or employer perspective.

Goldschmidt J, et al. *Future Oncol.* 2022; Epstein R, et al. *J Med Econ.* 2022; Hart L, et al. *Cancer Med.* 2023.



Economic Burden of Chemotherapy-Induced Myelosuppression

- Over the last 3 decades, studies have assessed the economic burden of CIM

Costs of Chemotherapy-Induced Myelosuppression		
	Direct Costs in 2021 USD ^a	Indirect Costs in 2021 USD
Neutropenia (per inpatient episode, including FN)	\$7,557 to \$77,909	\$7,400 to \$13,705 (per episode)
Neutropenia (per outpatient episode)	\$4108	N/A
Anemia management (per year)	\$35,547 to \$145,861	\$6,541 ^b (per year)
Anemia management (per treatment episode)	\$5,880 to \$27,369	N/A
Thrombocytopenia (per cycle or episode)	\$2,177 to \$11,917	\$8,264 (per episode)
Thrombocytopenia (per treatment episode)	\$8,544 to \$30,662	N/A

^aDirect and indirect costs from 2006 and 2010 were converted to 2021 costs using the medical care component of the Consumer Price Index from the US Bureau of Labor and Statistics.

^bIndirect costs reported for anemia were not adjusted for age, sex, comorbidities, and disease severity and included costs associated with absenteeism and short-term disability.

Liou S, et al. *Clin Drug Investig.* 2007; Wong W, et al. *PLoS One.* 2018; Epstein R, et al. *J Med Econ.* 2022.



Chemotherapy-Induced Neutropenia

- Common yet serious AE following myelosuppressive chemotherapy
- Risk factors can be
 - Patient specific
 - Disease specific
 - Treatment specific
- Neutropenia definitions:
 - Grade 3 = ANC $\geq 500/\mu\text{L}$ but $< 1,000/\mu\text{L}$
 - Grade 4 (severe) = ANC $< 500/\mu\text{L}$
- FN defined as a single oral temperature of $\geq 38.3\text{ }^\circ\text{C}$ (101 $^\circ\text{F}$) or $\geq 38.0\text{ }^\circ\text{C}$ (100.4 $^\circ\text{F}$) sustained over 1 hour and ANC $< 500/\mu\text{L}$ or an ANC that is expected to decline to $\leq 500/\mu\text{L}$ over the next 48 hours

Most common reason for dose delays/reductions, which can compromise patient outcomes

A 2012 national inpatient database showed **5.2% of all cancer-related hospitalizations are attributable to CIN**

Blayney D, et al. *Cancer Treat Rev.* 2022; Hart L, et al. *Cancer Med.* 2023; Boccia R, et al. *Oncologist.* 2022; NCCN Guidelines: Hematopoietic Growth Factors. Version 1.2025.

Select Tumor Types and Chemotherapy Regimens With Risk of CIN and/or FN



SCLC

Platinum/
Etoposide ± I/O^{a,b}

Topotecan^c

Lurbinectedin^{a,d}

Breast Cancer

DD AC → DD Paclitaxel^c

TAC^c

TC^c

TCH^c

Docetaxel^b; Paclitaxel Q21d^b

Colorectal Cancer

FOLFIRINOX^b

^aGrade 3/4 CIN
risk >20%.

^bFN risk 10%–20%.

^cFN risk >20%.

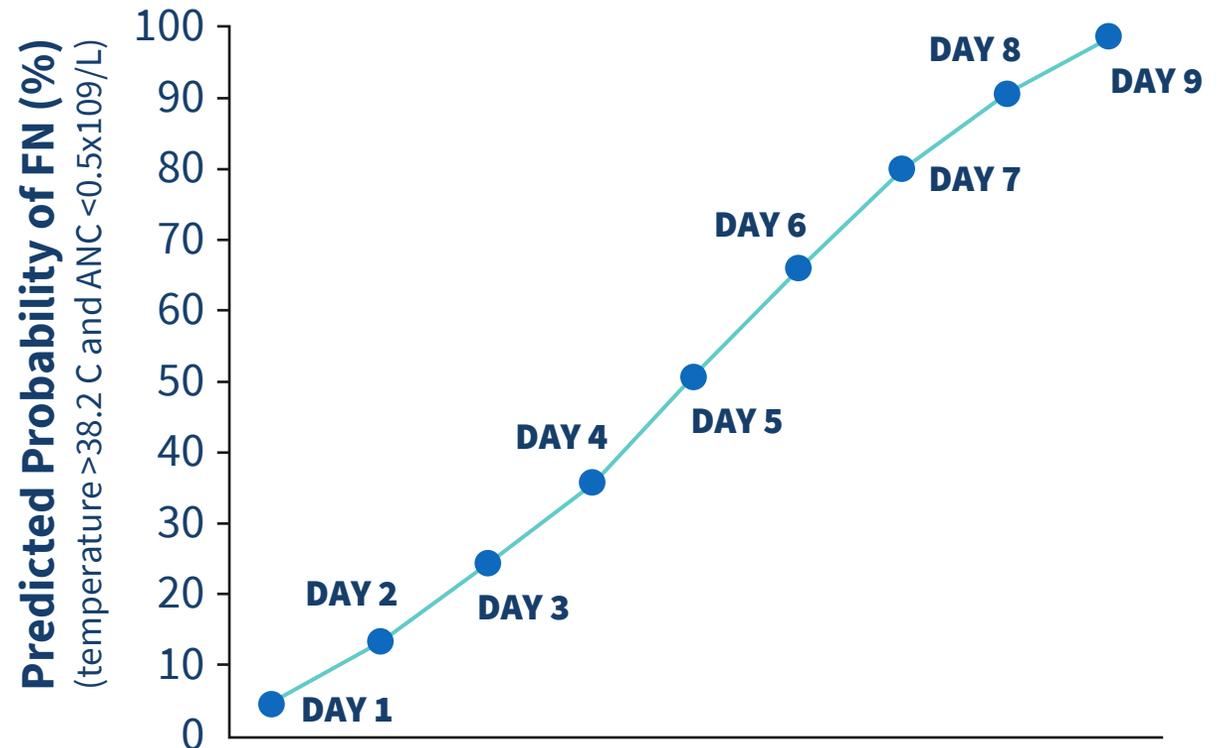
^dLurbinectedin is not recommended in the NCCN
Hematopoietic Growth Factor Guideline.

Consequences of Chemotherapy-Induced Neutropenia



- FN is associated with:
 - Prolonged hospitalization
 - Serious infections
 - Use of broad-spectrum antibiotics
 - Decreased QOL
 - Increased mortality
- The risk of infection **increases with duration** of severe neutropenia

Days of Severe Neutropenia

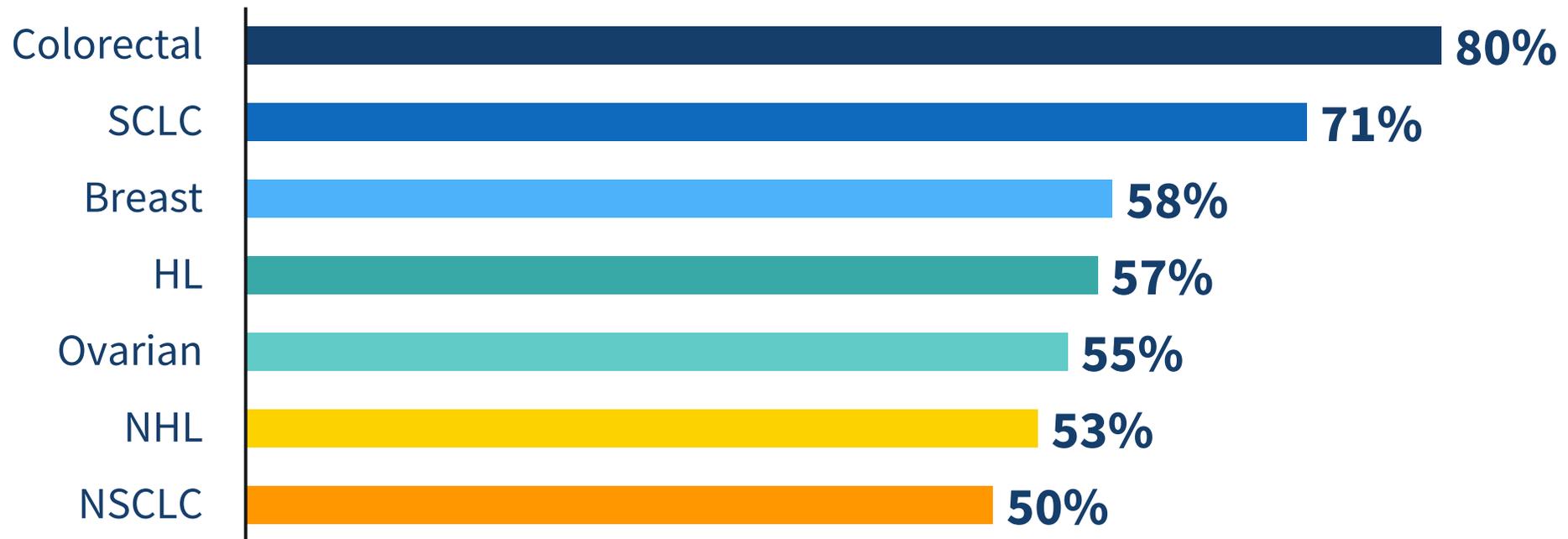


Adapted from Blackwell S, Crawford J. Filgrastim (r-metHuG-CSF) in the chemotherapy setting. In: Morstyn G, Dexter TM, eds. Filgrastim (r-metHuG-CSF) in Clinical Practice. Marcel Dekker, Inc; 1994:103-116; Blayney D, et al. *Cancer Treat Rev.* 2022; Hart L, et al. *Cancer Med.* 2023; Boccia R, et al. *Oncologist.* 2022; NCCN Guidelines: Hematopoietic Growth Factors. Version 1.2025.



Risk of Febrile Neutropenia is Greatest During Cycle 1 of Myelosuppressive Chemotherapy

Proportion of First FN Events in Cycle 1 by Cancer Type



Crawford J, et al. *J Natl Compr Canc Netw*. 2008.



Chemotherapy-Induced Anemia (CIA)

- CIA is common, occurring in 30%–90% of patients
- Incidence is highly variable
- In addition to tumor type and regimen, risk factors for CIA include older age, comorbidities, and poor performance status
- Hemoglobin (Hb) level ≤ 11 g/dL should prompt an evaluation in cancer patients
- In patients with high baseline Hb level, a drop of ≥ 2 g/dL may be cause for concern and assessment

Natalucci V, et al. *Nutrients*. 2021; Bryer E, et al. *Int J Clin Transfusion Med*. 2018; NCCN Guidelines: Hematopoietic Growth Factors. Version 1.2025; Rodgers G, et al. *J Natl Compr Cancer Netw*. 2012; Bohlius J, et al. *J Clin Oncol*. 2019; Aapro M, et al. *Ann Oncol*. 2018; Crawford J, et al. *Future Oncol*. 2024.

Select Tumor Types and Chemotherapy Regimens Associated With >20% Incidence of \geq Grade 2 Anemia in Clinical Trials



Breast

- AC
- TAC
- AC \rightarrow Paclitaxel
- TC
- TCH^a

Colorectal

- CAPOX
- FOLFOX

NSCLC/SCLC

- Carboplatin/
Paclitaxel
- Platinum/Etoposide
 \pm I/O^a
- Cisplatin/
Pemetrexed^a
- Topotecan^a

Ovarian

- Carboplatin/
Paclitaxel^a

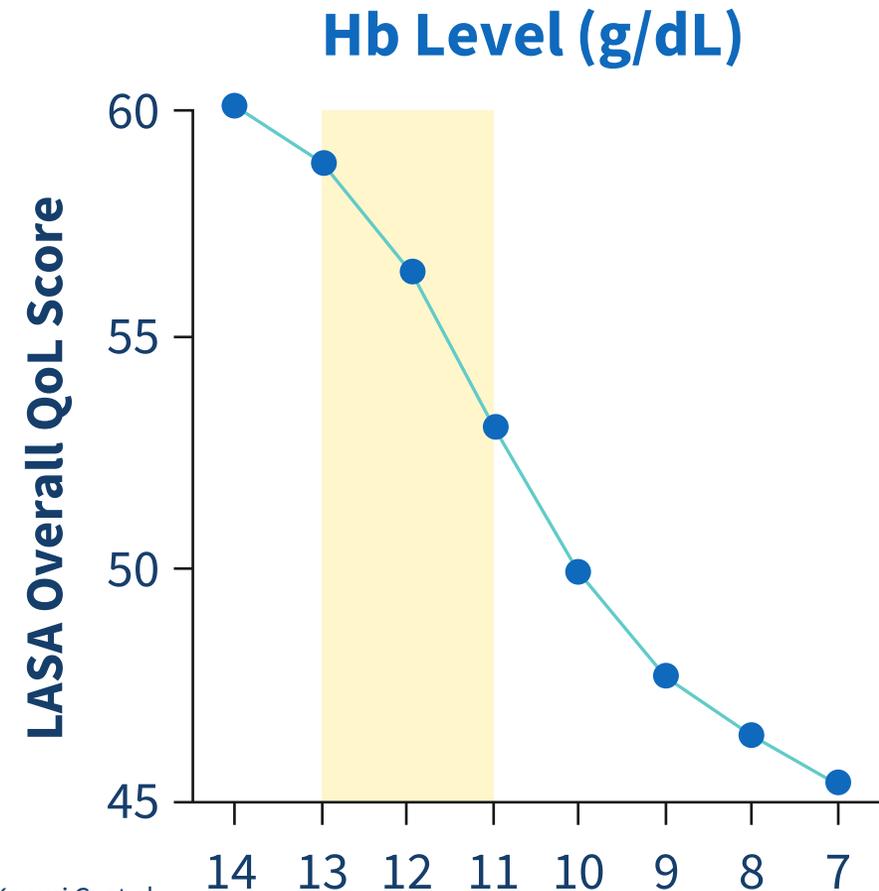
^aRegimens with >10% incidence of \geq Grade 3 anemia.

Hart L, et al. *Cancer Med.* 2023; NCCN Guidelines: Hematopoietic Growth Factors. Version 1.2025; Rodgers G, et al. *J Natl Compr Cancer Netw.* 2012; Bohlius J, et al. *J Clin Oncol.* 2019; Apro M, et al. *Ann Oncol.* 2018; Crawford J, et al. *Future Oncol.* 2024.



Hemoglobin Level is Associated with QOL

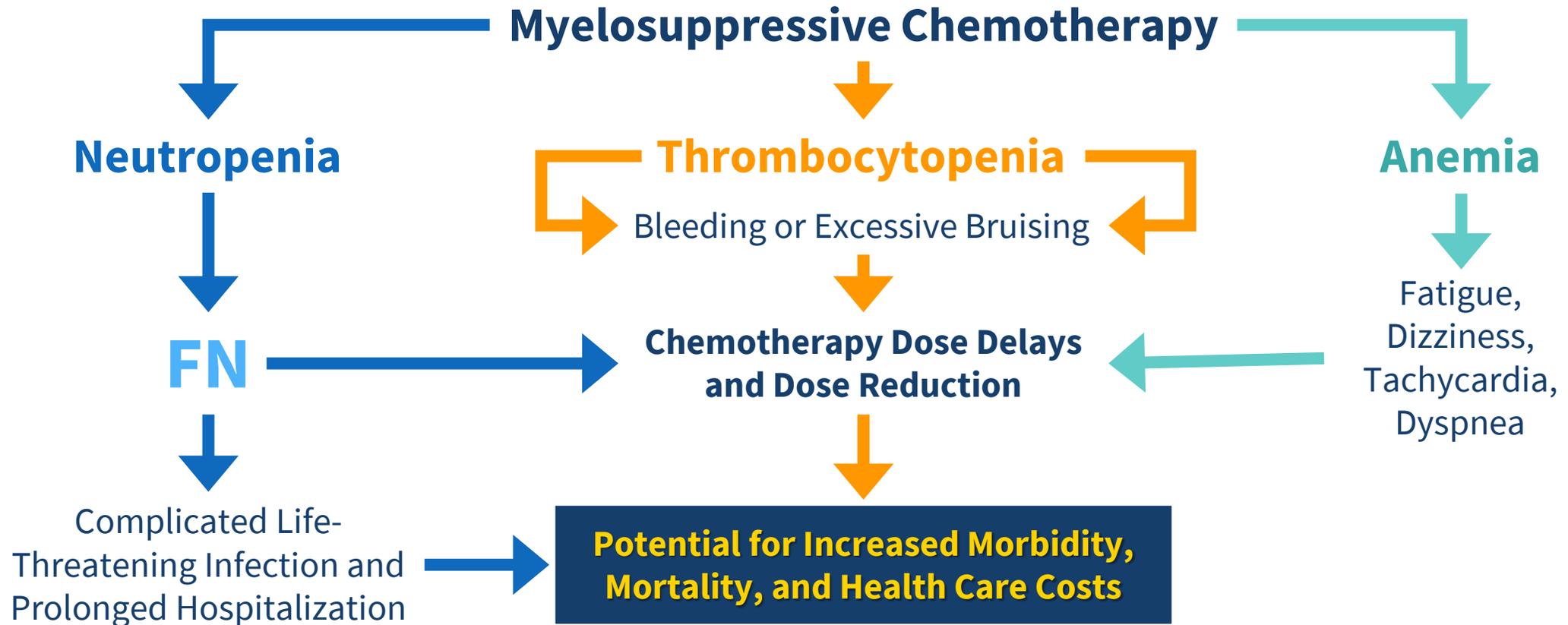
- CIA can cause
 - Fatigue
 - Depression
 - Dyspnea
 - Tachycardia
 - Drowsiness
 - Dizziness
- **Higher Hb levels are associated with better QOL** 
- Consequences of CIA can lead to chemotherapy delays and a negative effect on QOL
- CIA associated with increased morbidity, mortality, and healthcare costs



Rodgers GM. *Expert Rev Hematol.* 2024; Gilreath JA, et al. *Am J Hematol.* 2014; Crawford J, et al. *Cancer.* 2002; Kanuri G, et al. *PLoS One.* 2016; Auerbach M, et al. *J Clin Oncol.* 2004; Rodgers GM, et al. *Acta Haematol.* 2019; Gilreath J, et al. *Blood.* 2020.



Consequences of Myelosuppressive Chemotherapy



Goldschmidt J, et al. *Future Oncol.* 2022; Epstein R, et al. *J Med Econ.* 2022; Hart L, et al. *Cancer Med.* 2023; Epstein R, et al. *Adv Ther.* 2020; NCCN Clinical Practice Guideline: Hematopoietic Growth Factors. Version 1.2025; Rodgers G, et al. *J Natl Compr Cancer Netw.* 2012; Rodgers GM. *Expert Rev Hematol.* 2024; Gilreath JA, et al. *Am J Hematol.* 2014; Crawford J, et al. *Cancer.* 2002; Kanuri G, et al. *PLoS One.* 2016.

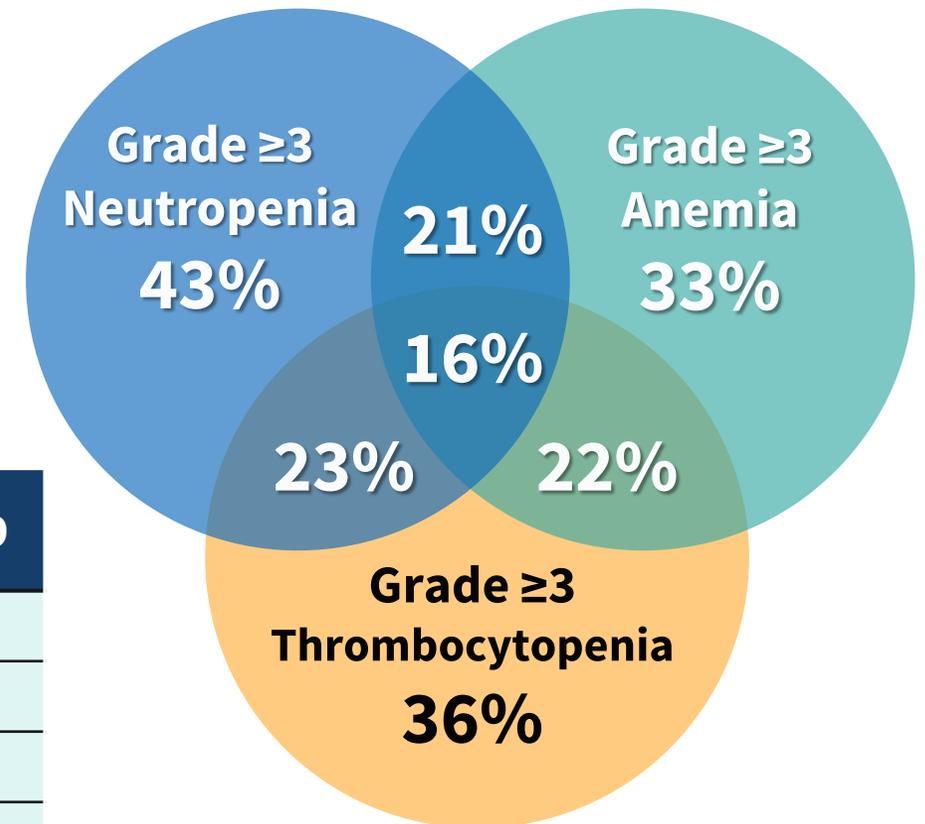


Chemotherapy Can Affect Multiple Blood Cell Lineages Requiring Substantial Supportive Care

- Retrospective cohort study
 - EMR data from Florida Cancer Specialists & Research Institute
 - Jan 2013–Dec 2020; **1,239 patients with ES-SCLC treated with chemotherapy**
 - Burden of myelosuppression and supportive care

- Grade ≥ 3 AEs in:
 - ≥ 1 lineage: 62.1%
 - ≥ 2 lineages: 33.9%
 - 3 lineages: 15.5%

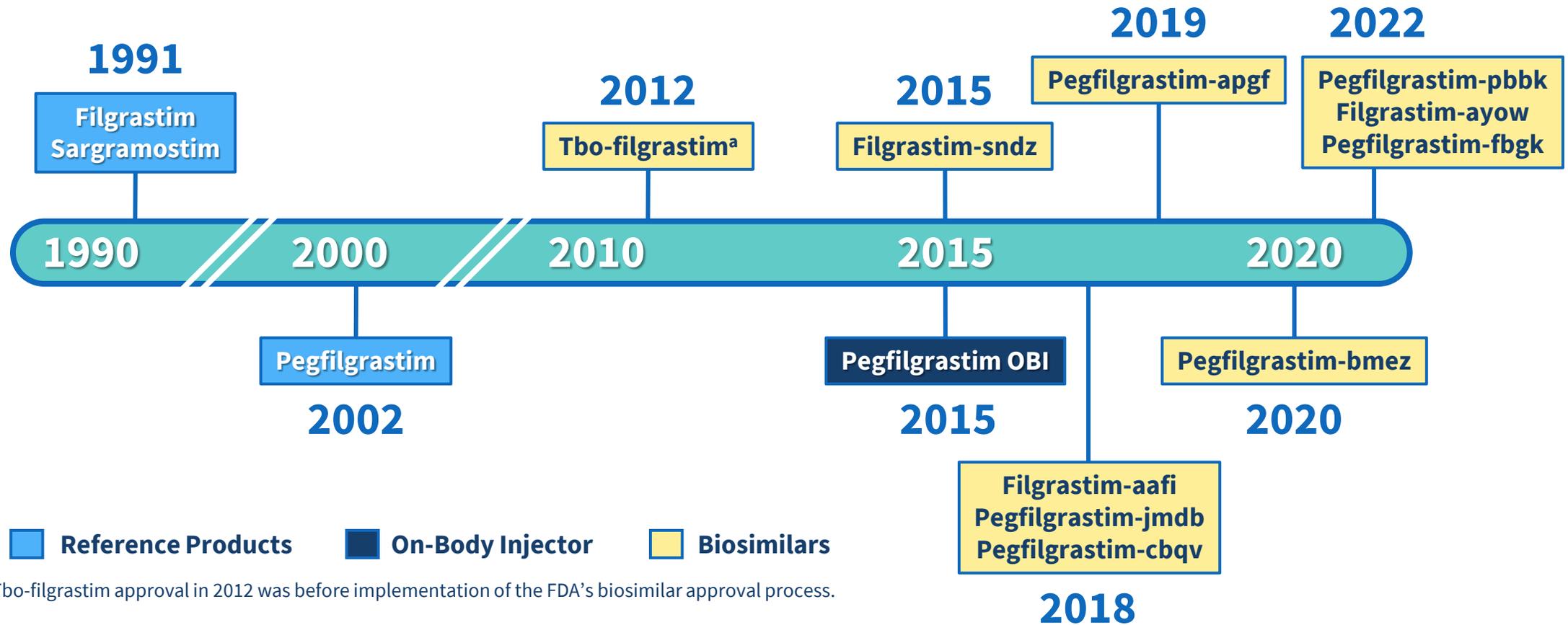
Supportive Care Interventions	N=1239
G-CSF	89.7%
ESA	24.4%
RBC Transfusion	32.6%
Platelet Transfusion	3.7%



Hart L, et al. *Cancer Med.* 2023.



FDA-Approved WBC Growth Factors



^aTbo-filgrastim approval in 2012 was before implementation of the FDA's biosimilar approval process.

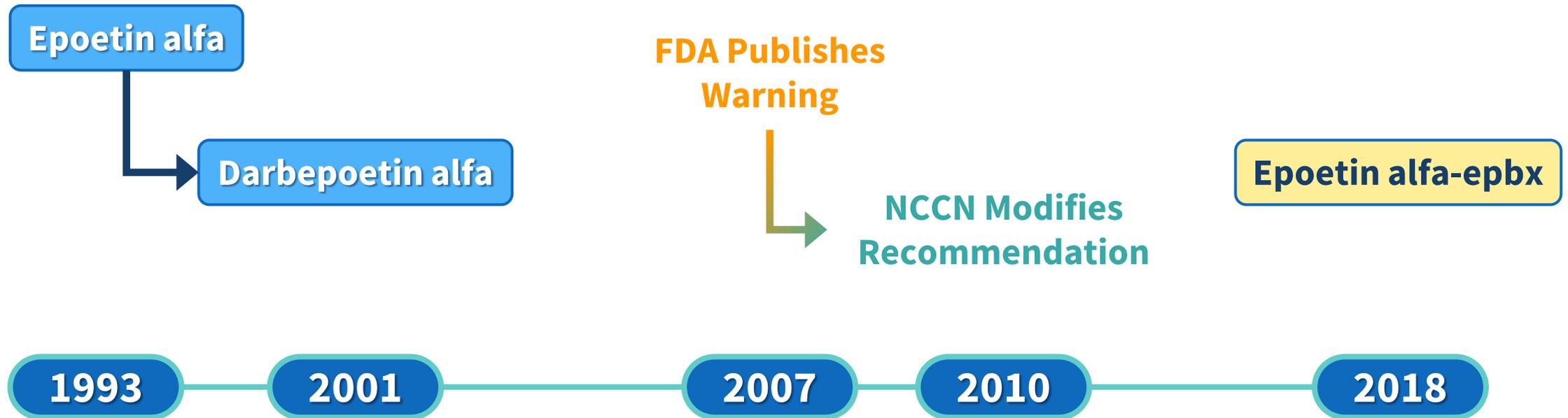
Cuellar S, et al. *Am J Health Syst Pharm.* 2019; FDA Prescribing Information.



FDA-Approved Erythropoiesis-Stimulating Agents

■ Reference Products

■ Biosimilar



Manns B, et al. *CJASN*. 2012; NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025; Rodgers G, et al. *J Natl Compr Cancer Netw*. 2012; Bohlius J, et al. *J Clin Oncol*. 2019; Aapro M, et al. *Ann Oncol*. 2018; Crawford J, et al. *Future Oncol*. 2024; FDA Prescribing Information.



ASCO/ASH Recommendations for ESAs

- Consider ESAs for patients whose cancer treatment is not curative in intent AND Hb level is <10 g/dL
- For patients with multiple myeloma, NHL, or CLL, clinicians should observe the hematologic response to chemotherapy before considering ESA therapy
- Increase Hb level to the lowest concentration needed to avoid or reduce the need for RBC transfusion
- ESA therapy should be discontinued in patients who do not respond within 6 to 8 weeks
- Iron replacement can be used in conjunction with ESAs in patients with and without iron deficiency

Bohlius J, et al. *J Clin Oncol*. 2019.



ASCO Recommendations for Platelet Transfusions

Prophylactic versus therapeutic platelet transfusions

- Prophylactic transfusions should be administered to patients with impaired bone marrow function to reduce the risk of hemorrhage

Thresholds for prophylactic platelet transfusions

- Recommended threshold for solid tumors and hematologic malignancies is $<10 \times 10^9/L$
 - **Solid tumors:**
 - Risk of bleeding is related to the depth and duration of the platelet nadir
 - Higher threshold is appropriate for active localized bleeding
 - **Hematologic malignancies:**
 - Higher threshold may be advisable in certain circumstances

Schiffer C, et al. *J Clin Oncol*. 2018.



Extensive-Stage SCLC is Managed With Myelosuppressive Chemotherapy Regimens

Current Treatments and Challenges

- **Neutropenia**
 - G-CSFs can cause bone pain
- **Anemia**
 - RBC transfusions result in rapid improvement in Hb but may require additional office visits
 - No universal RBC transfusion criteria exist
- **Thrombocytopenia**
 - Generally managed with platelet transfusions or dose delays and/or reductions
 - No FDA-approved therapy is available for CIT

Incidence of Grade 3/4 Toxicity	First-line Platinum/Etoposide	First-line Platinum/Etoposide + I/O Agent	Second-line Topotecan
Neutropenia	25%-48%	23%-45%	54%
Anemia	12%-22%	13%-17%	31%
Thrombocytopenia	8%-17%	10%-20%	54%

For patients with ES-SCLC, treatment focuses on prolonging survival and improving quality of life

Abbreviations: CIT=chemotherapy-induced thrombocytopenia; ES=extensive-stage; G-CSF=granulocyte colony-stimulating factor; I/O=immuno-oncology; RBC=red blood cell; SCLC=small cell lung cancer.

Goldschmidt J, et al. *Future Oncol.* 2022; Epstein R, et al. *Adv Ther.* 2020; Crawford J, et al. *Future Oncol.* 2024; Hart L, et al. *Cancer Med.* 2023; NCCN Guidelines: Hematopoietic Growth Factors. Version 1.2025; NCCN Clinical Practice Guidelines: Small Cell Lung Cancer. Version 2.2026; Kalemkerian G, et al. *J Clin Oncol.* 2025.



The ABCs of ES-SCLC

An Overview of Current and Evolving Standards of Care

NCCN: 1st-Line Standard of Care for ES-SCLC



4 cycles of cytotoxic chemotherapy are recommended, but some patients may receive up to 6 cycles based on response and tolerability after 4 cycles.

Preferred Regimens

- **Carboplatin + etoposide + atezolizumab** followed by maintenance atezolizumab
- **Carboplatin + etoposide + durvalumab** followed by maintenance durvalumab
- **Cisplatin + etoposide + durvalumab** followed by maintenance durvalumab

NCCN Clinical Practice Guidelines: Small Cell Lung Cancer. Version 2.2026.



NCCN: 1st-Line Standard of Care for ES-SCLC

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Other Recommended Regimens

- **Carboplatin + etoposide**
- **Cisplatin + etoposide**

NCCN Clinical Practice Guidelines: Small Cell Lung Cancer. Version 2.2026.



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Other Recommended Regimens

- **Carboplatin + etoposide**
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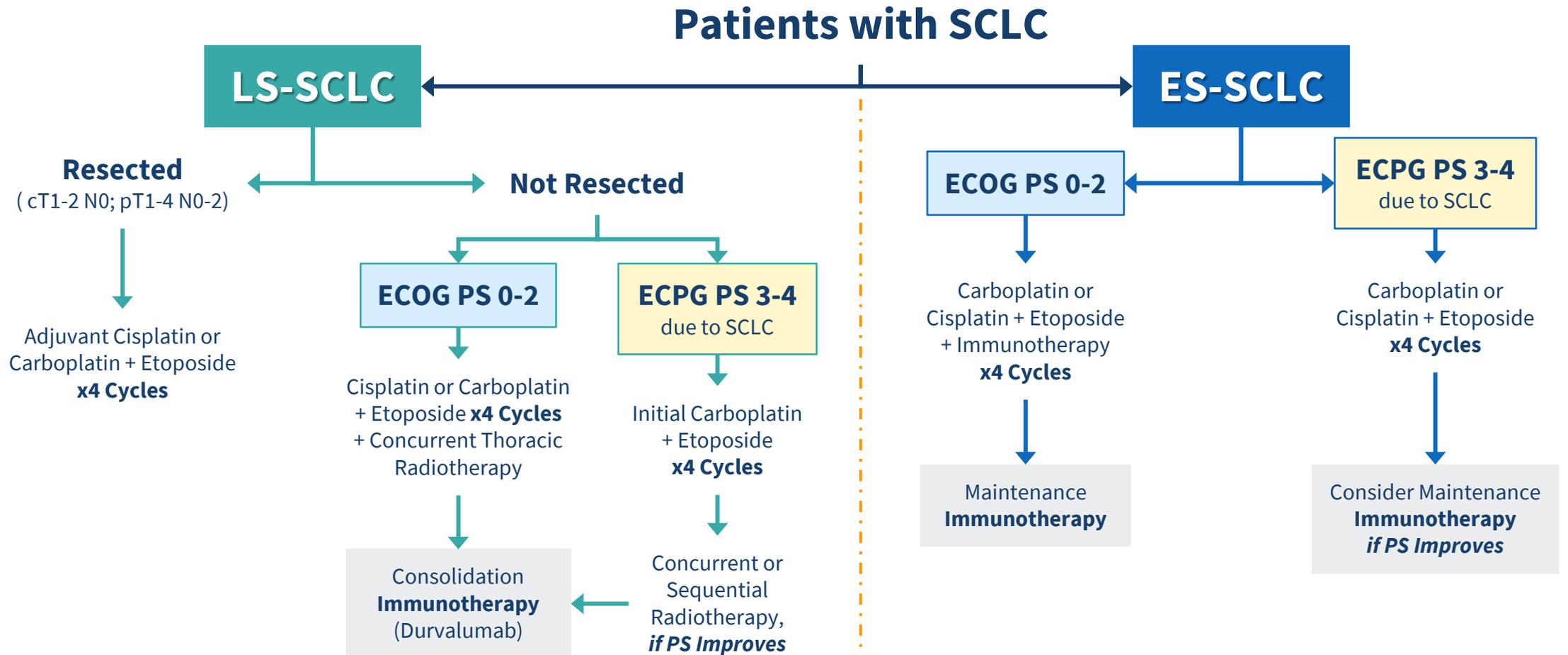
Useful in Certain Circumstances

- **Carboplatin + irinotecan**
- **Cisplatin + irinotecan**

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ASCO: Systemic Therapy for SCLC



Kalemkerian G, et al. *J Clin Oncol*. 2025.

Consider dose reduction or growth factor support for patients with PS 2.



NCCN: Subsequent Systemic Therapy (PS 0-2)

CTFI >6 Months

Preferred Regimens

- Clinical trial enrollment
- Re-treatment with platinum-based doublet

Other Recommended Regimens

- Lurbinectedin
- Irinotecan
- Topotecan oral (PO) or intravenous (IV)
- Tarlatamab-dlle

CTFI: Chemotherapy-Free Interval

NCCN Clinical Practice Guidelines: Small Cell Lung Cancer. Version 2.2026

Consider dose reduction or growth factor support for patients with PS 2.



NCCN: Subsequent Systemic Therapy (PS 0-2)

CTFI >6 Months

Preferred Regimens

- Clinical trial enrollment
- Re-treatment with platinum-based doublet

Other Recommended Regimens

- Lurbinectedin
- Topotecan oral (PO) or intravenous (IV)
- Irinotecan
- Tarlatamab-dlle

CTFI: Chemotherapy-Free Interval

CTFI ≤6 Months

Preferred Regimens

- Clinical trial enrollment
- Lurbinectedin
- Topotecan oral (PO) or intravenous (IV)
- Irinotecan
- Tarlatamab-dlle
- Re-treatment with platinum-based doublet may be considered for CTFI 3-6 months

Other Recommended Regimens

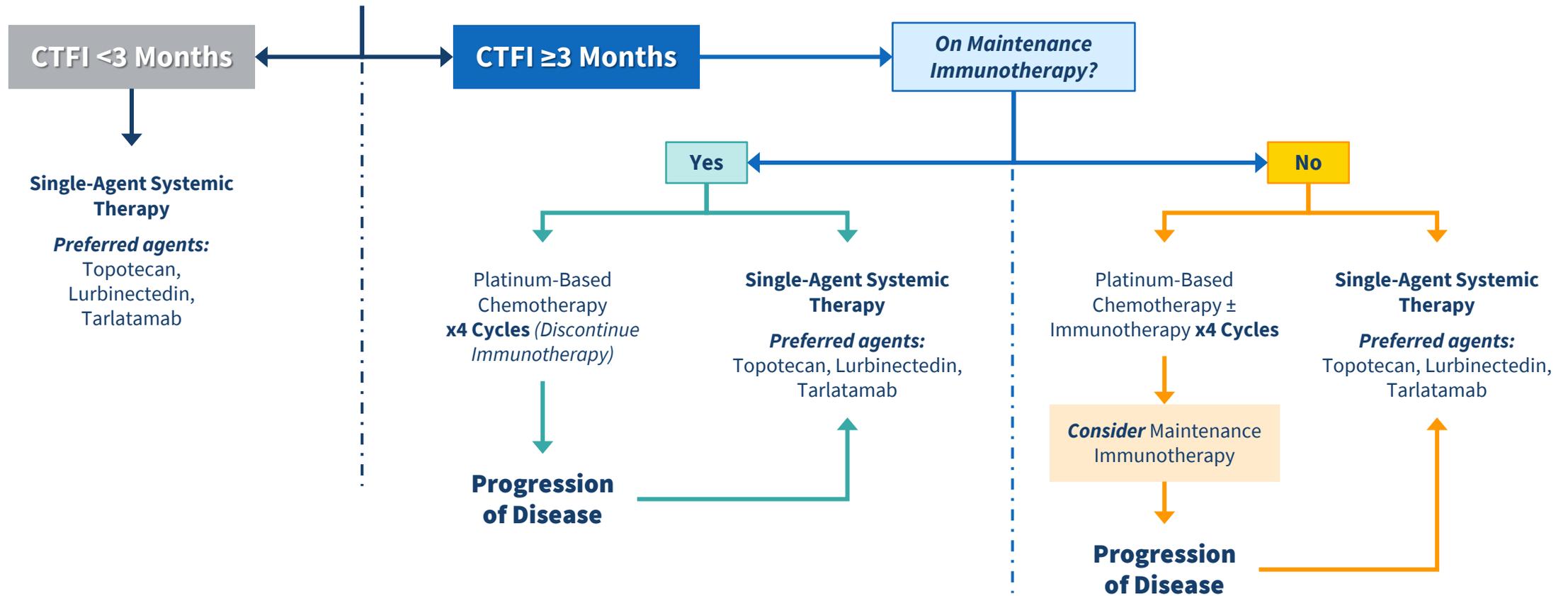
- Nivolumab or pembrolizumab (if not previously treated with an ICI)
- Paclitaxel
- Temozolomide
- Cyclophosphamide/doxorubicin/vincristine (CAV)
- Docetaxel
- Gemcitabine
- Etoposide (oral)

NCCN Clinical Practice Guidelines: Small Cell Lung Cancer. Version 2.2026



ASCO: Systemic Therapy for Relapsed SCLC

Patients With Relapsed SCLC



Kalemkerian G, et al. *J Clin Oncol*. 2025.



First-Line Atezolizumab Plus Chemotherapy in Extensive-Stage Small-Cell Lung Cancer

Leora **Horn**, M.D., Aaron S. **Mansfield**, M.D., Aleksandra **Szczęsna**, M.D., Libor **Havel**, M.D., Maciej **Krzakowski**, M.D., Ph.D., Maximilian J. **Hochmair**, M.D., Florian **Huemer**, M.D., György **Losonczy**, M.D., Ph.D., Melissa L. **Johnson**, M.D., Makoto **Nishio**, M.D., Ph.D., Martin **Reck**, M.D., Tony **Mok**, M.D., Sivuonthanh **Lam**, Pharm.D., David S. **Shames**, Ph.D., Juan **Liu**, Ph.D., Beiyong **Ding**, Ph.D., Ariel **Lopez-Chavez**, M.D., Fairouz **Kabbinavar**, M.D., Wei **Lin**, M.D., Alan **Sandler**, M.D., Stephen V. **Liu**, M.D., for the **IMpower133 Study Group**

N Engl J Med
Volume 379(23):2220-2229
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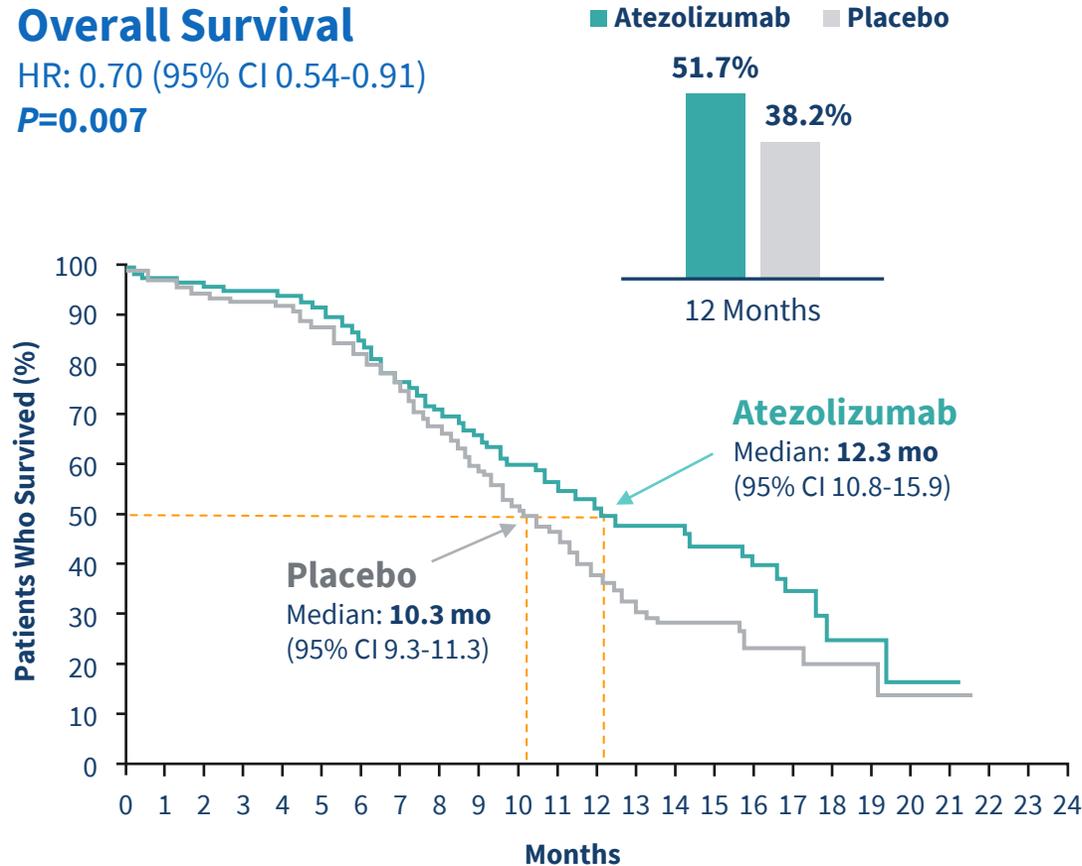


Overall Survival & Progression-Free Survival

Overall Survival

HR: 0.70 (95% CI 0.54-0.91)

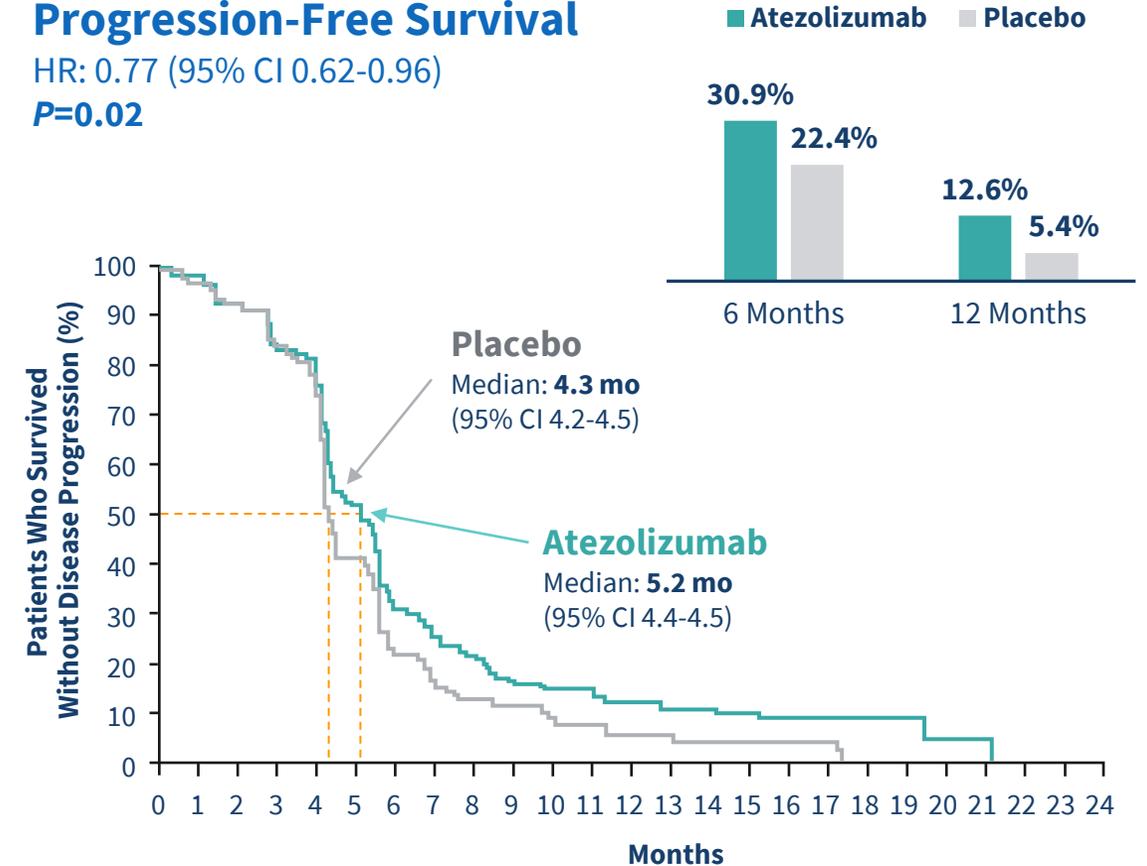
P=0.007



Progression-Free Survival

HR: 0.77 (95% CI 0.62-0.96)

P=0.02

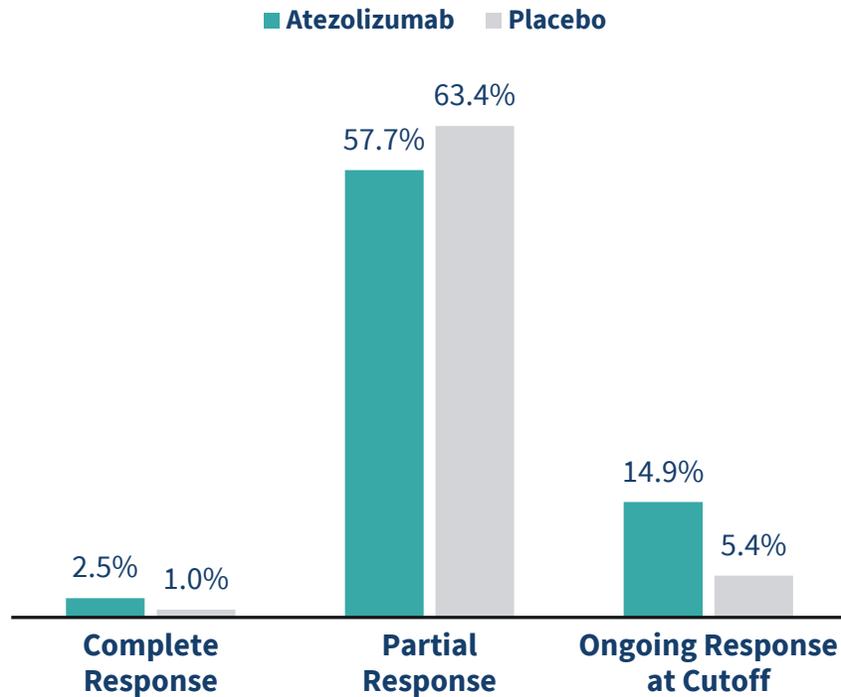


Horn L, et al. *N Engl J Med.* 2018.

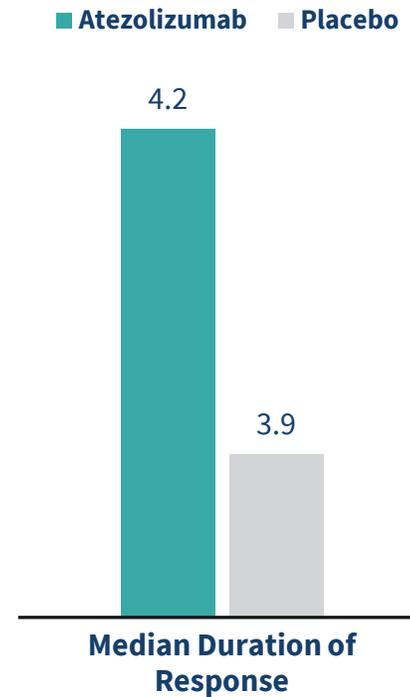


Response to Treatment

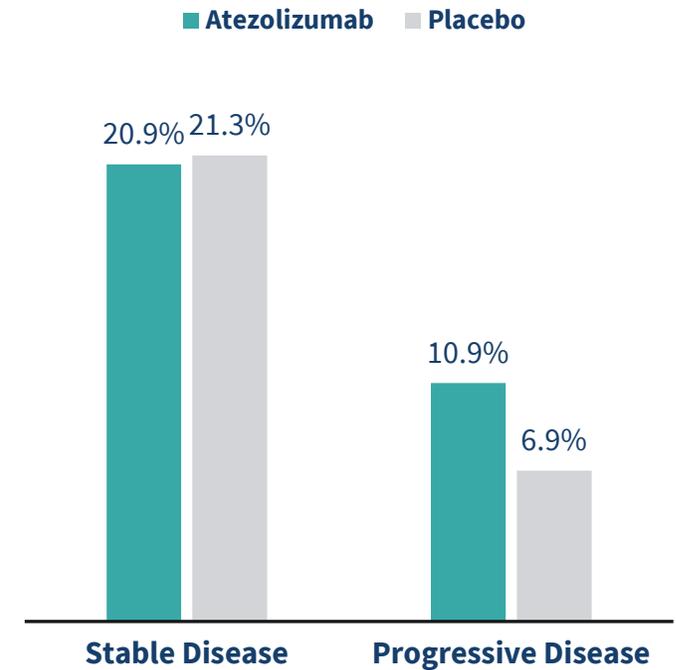
Objective Confirmed Response (%)



Median Duration of Response (mos)



Disease Progression (%)



Horn L, et al. *N Engl J Med*. 2018.



Adverse Events Related to the Trial Regimen

Neutropenia

Grade 1: $\geq 1,500$ to $< 2,000/\mu\text{L}$

Grade 2: $\geq 1,000$ to $< 1,500/\mu\text{L}$

Grade 3: ≥ 500 to $< 1,000/\mu\text{L}$

Grade 4: $< 500/\mu\text{L}$

Anemia

Grade 1: Hgb $< \text{LLN}$ ≥ 10.0 g/dL

Grade 2: Hgb 8.0 to < 10.0 g/dL

Grade 3: Hgb 6.5 to < 8.0 g/dL

Grade 4: Hgb < 6.5 g/dL

Thrombocytopenia

Grade 1: $< \text{LLN}$ to $75\text{k}/\mu\text{L}$

Grade 2: $< 75\text{k}$ to $50\text{k}/\mu\text{L}$

Grade 3: $< 50\text{k}$ to $25\text{k}/\mu\text{L}$

Grade 4: $< 25\text{k}/\mu\text{L}$

Event	Atezolizumab (N=198), No. of Patients (%)			Placebo (N=196), No. of Patients (%)		
	Grade 1 or 2	Grade 3 or 4	Grade 5	Grade 1 or 2	Grade 3 or 4	Grade 5
Any Adverse Event	73 (36.9)	112 (56.6)	3 (1.5)	68 (34.7)	110 (56.1)	3 (1.5)
Adverse Events With Incidence $\geq 10\%$ (Any Category) or $\geq 2\%$ (Grade 3 or 4)						
Neutropenia	26 (13.1)	45 (22.7)	1 (0.5)	20 (10.2)	48 (24.5)	0
Anemia	49 (24.7)	28 (14.1)	0	41 (20.9)	24 (12.2)	0
Alopecia	69 (34.8)	0	0	66 (33.7)	0	0
Nausea	62 (31.1)	1 (0.5)	0	58 (29.6)	1 (0.5)	0
Fatigue	39 (19.7)	3 (1.5)	0	37 (18.9)	1 (0.5)	0
Decreased Neutrophil Count	7 (3.5)	28 (14.1)	0	12 (6.1)	33 (16.8)	0
Decreased Appetite	39 (19.7)	2 (1.0)	0	26 (13.3)	0	0
Thrombocytopenia	12 (6.1)	20 (10.1)	0	14 (7.1)	15 (7.7)	0
Decreased Platelet Count	17 (8.6)	7 (3.5)	0	21 (10.7)	7 (3.6)	0
Vomiting	25 (12.6)	2 (1.0)	0	19 (9.7)	3 (1.5)	0
Constipation	19 (9.6)	1 (0.5)	0	25 (12.8)	0	0
Leukopenia	15 (7.6)	10 (5.1)	0	10 (5.1)	8 (4.1)	0
Decreased White-Cell Count	10 (5.1)	6 (3.0)	0	16 (8.2)	9 (4.6)	0
Diarrhea	15 (7.6)	4 (2.0)	0	18 (9.2)	1 (0.5)	0
Febrile Neutropenia	0	6 (3.0)	0	0	12 (6.1)	0
Infusion-Related Reaction	6 (3.0)	4 (2.0)	0	9 (4.6)	1 (0.5)	0

Horn L, et al. *N Engl J Med.* 2018.



Adverse Events Related to the Trial Regimen

Neutropenia

Grade 1: $\geq 1,500$ to $< 2,000/\mu\text{L}$

Grade 2: $\geq 1,000$ to $< 1,500/\mu\text{L}$

Grade 3: ≥ 500 to $< 1,000/\mu\text{L}$

Grade 4: $< 500/\mu\text{L}$

Anemia

Grade 1: Hgb $< \text{LLN} \geq 10.0$ g/dL

Grade 2: Hgb 8.0 to < 10.0 g/dL

Grade 3: Hgb 6.5 to < 8.0 g/dL

Grade 4: Hgb < 6.5 g/dL

Thrombocytopenia

Grade 1: $< \text{LLN}$ to $75\text{k}/\mu\text{L}$

Grade 2: $< 75\text{k}$ to $50\text{k}/\mu\text{L}$

Grade 3: $< 50\text{k}$ to $25\text{k}/\mu\text{L}$

Grade 4: $< 25\text{k}/\mu\text{L}$

Event	Atezolizumab (N=198), No. of Patients (%)			Placebo (N=196), No. of Patients (%)		
	Grade 1 or 2	Grade 3 or 4	Grade 5	Grade 1 or 2	Grade 3 or 4	Grade 5
Any Adverse Event	73 (36.9)	112 (56.6)	3 (1.5)	68 (34.7)	110 (56.1)	3 (1.5)
Adverse Events With Incidence $\geq 10\%$ (Any Category) or $\geq 2\%$ (Grade 3 or 4)						
Neutropenia	26 (13.1)	45 (22.7)	1 (0.5)	20 (10.2)	48 (24.5)	0
Anemia	49 (24.7)	28 (14.1)	0	41 (20.9)	24 (12.2)	0
Alopecia	69 (34.8)	0	0	66 (33.7)	0	0
Nausea	62 (31.1)	1 (0.5)	0	58 (29.6)	1 (0.5)	0
Fatigue	39 (19.7)	3 (1.5)	0	37 (18.9)	1 (0.5)	0
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Febrile Neutropenia	0	6 (3.0)	0	0	12 (6.1)	0
Infusion-Related Reaction	6 (3.0)	4 (2.0)	0	9 (4.6)	1 (0.5)	0

Horn L, et al. *N Engl J Med.* 2018.



Adverse Events Related to the Trial Regimen

Neutropenia

Grade 1: $\geq 1,500$ to $< 2,000/\mu\text{L}$

Grade 2: $\geq 1,000$ to $< 1,500/\mu\text{L}$

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Anemia

Grade 1: Hgb $< \text{LLN} \geq 10.0$ g/dL

Grade 2: Hgb 8.0 to < 10.0 g/dL

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Grade 4: Hgb < 6.5 g/dL

Thrombocytopenia

Grade 1: $< \text{LLN}$ to $75\text{k}/\mu\text{L}$

Grade 2: $< 75\text{k}$ to $50\text{k}/\mu\text{L}$

Grade 3: $< 50\text{k}$ to $25\text{k}/\mu\text{L}$

Grade 4: $< 25\text{k}/\mu\text{L}$

Event	Atezolizumab (N=198), No. of Patients (%)			Placebo (N=196), No. of Patients (%)		
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Adverse Events Related to the Trial Regimen

Neutropenia

Grade 1: $\geq 1,500$ to $< 2,000/\mu\text{L}$

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Grade 4: Hgb < 6.5 g/dL

Thrombocytopenia

Grade 1: $< \text{LLN}$ to $75\text{k}/\mu\text{L}$

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Infusion-Related Reaction	6 (3.0)	4 (2.0)	0	9 (4.6)	1 (0.5)	0

Horn L, et al. *N Engl J Med.* 2018.



Adverse Events Related to the Trial Regimen

Neutropenia

- Grade 1:** $\geq 1,500$ to $< 2,000/\mu\text{L}$
- Grade 2:** $\geq 1,000$ to $< 1,500/\mu\text{L}$
- Grade 3:** ≥ 500 to $< 1,000/\mu\text{L}$
- Grade 4:** $< 500/\mu\text{L}$

Anemia

- Grade 1:** Hgb $< \text{LLN}$ ≥ 10.0 g/dL
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Thrombocytopenia

- Grade 1:** $< \text{LLN}$ to $75\text{k}/\mu\text{L}$
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Anemia	49 (24.7)	28 (14.1)	0	41 (20.9)	24 (12.2)	0
Alopecia	69 (34.8)	0	0	66 (33.7)	0	0
Nausea	62 (31.1)	1 (0.5)	0	58 (29.6)	1 (0.5)	0
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Decreased Neutrophil Count	7 (3.5)	28 (14.1)	0	12 (6.1)	33 (16.8)	0
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Thrombocytopenia	12 (6.1)	20 (10.1)	0	14 (7.1)	15 (7.7)	0
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Vomiting	25 (12.6)	2 (1.0)	0	19 (9.7)	3 (1.5)	0
Constipation	19 (9.6)	1 (0.5)	0	25 (12.8)	0	0
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Diarrhea	15 (7.6)	4 (2.0)	0	18 (9.2)	1 (0.5)	0
Febrile Neutropenia	0	6 (3.0)	0	0	12 (6.1)	0
Infusion-Related Reaction	6 (3.0)	4 (2.0)	0	9 (4.6)	1 (0.5)	0

Horn L, et al. *N Engl J Med.* 2018.



Durvalumab Plus Platinum-Etoposide Versus Platinum-Etoposide in First-Line Treatment of Extensive-Stage Small-Cell Lung Cancer (CASPIAN): a Randomised, Controlled, Open-Label, Phase 3 Trial

Luis **Paz-Ares**, Mikhail **Dvorkin**, Yuanbin **Chen**, Niels **Reinmuth**, Katsuyuki **Hotta**, Dmytro **Trukhin**, Galina **Statsenko**, Maximilian J **Hochmair**, Mustafa **Özgüroğlu**, Jun **Ho Ji**, Oleksandr **Voitko**, Artem **Poltoratskiy**, Santiago **Ponce**, Francesco **Verderame**, Libor **Havel**, Igor **Bondarenko**, Andrzej **Kazarnowicz**, György **Losonczy**, Nikolay V **Conev**, Jon **Armstrong**, Natalie **Byrne**, Norah **Shire**, Haiyi **Jiang**, Jonathan W **Goldman**, for the **CASPIAN Investigators**

Lancet 2019; 394: 1929-39

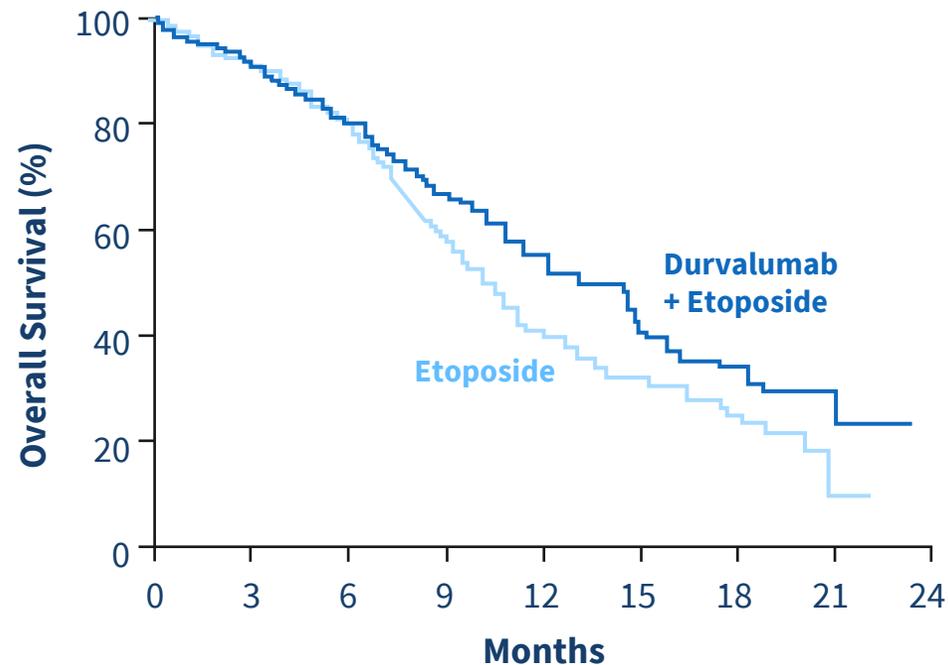


Overall Survival & Progression-Free Survival

Overall Survival

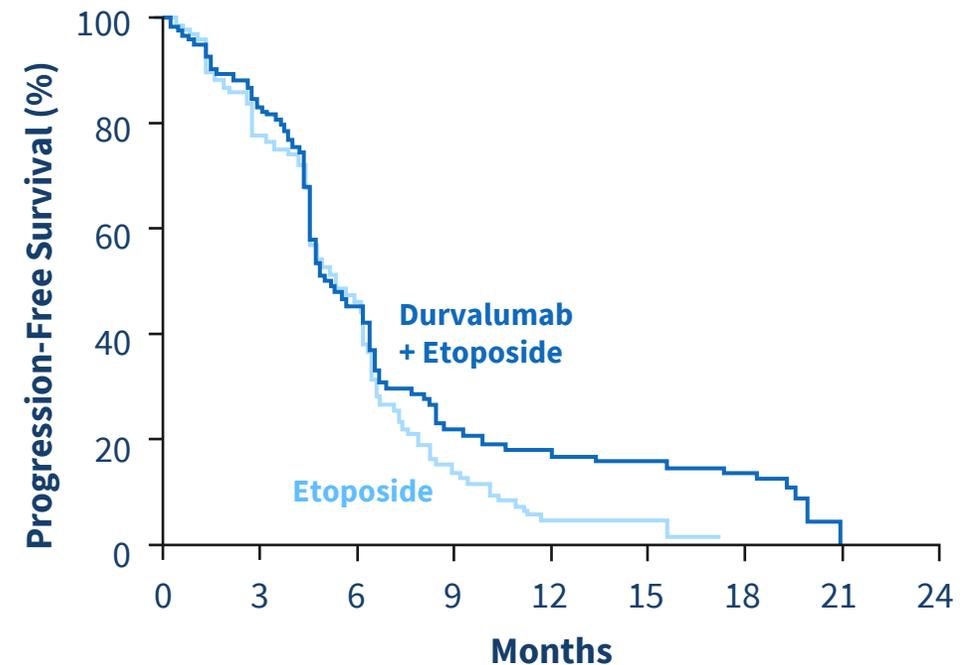
HR: 0.73 (95% CI 0.59-0.91)

P=0.0047



Progression-Free Survival

HR: 0.78 (95% CI 0.65-0.94)

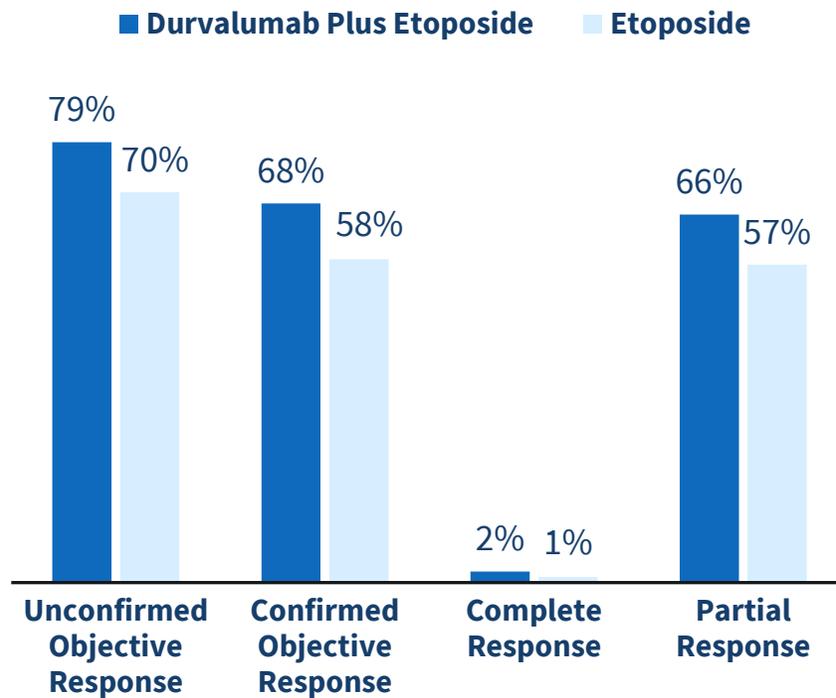


Paz-Ares L, et al. *N Engl J Med*. 2019.

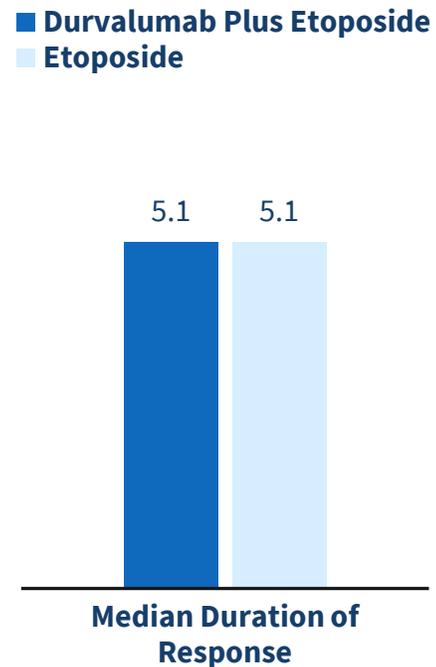


Response to Treatment

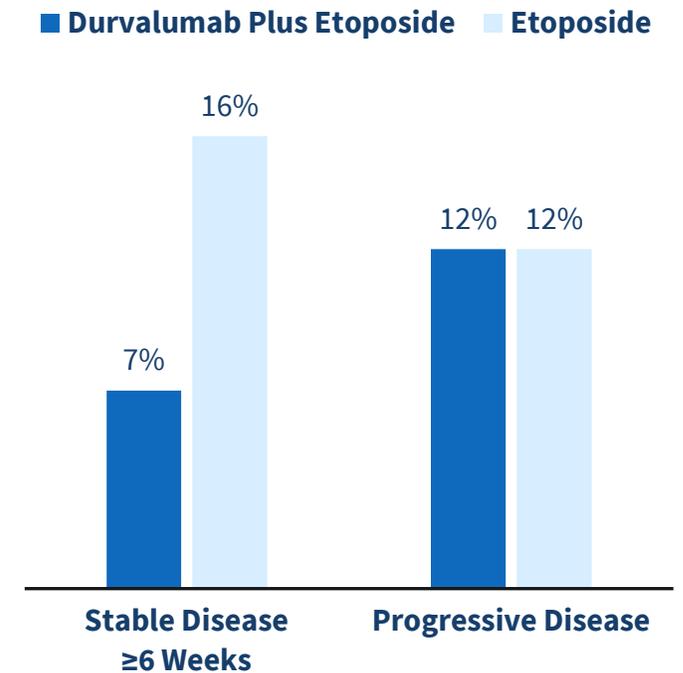
Response Rates (%)



Median Duration of Response (Months)



Disease Progression (%)



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Adverse Events Related to the Trial Regimen

Event	Durvalumab Plus Etoposide (N=265), No. of Patients (%)		Etoposide (N=266), No. of Patients (%)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Any Adverse Event	260 (98)	163 (62)	258 (97)	166 (62)
Any Serious Event	82 (31)	57 (22)	96 (36)	70 (26)
Any Event Leading to Discontinuation	25 (9)	7 (3)	25 (9)	7 (3)
Any Event Leading to Death	13 (5)	--	15 (6)	--
Any Events With Incidence \geq 10% (Any Grade) or \geq 2% (Grade 3 or 4)				
Neutropenia	111 (42)	64 (24)	124 (47)	88 (33)
Anemia	102 (38)	24 (9)	125 (47)	48 (18)
Nausea	89 (34)	1 (<1)	89 (33)	5 (2)
Alopecia	83 (31)	3 (1)	91 (34)	2 (1)
Constipation	44 (17)	2 (1)	51 (19)	0
Decreased Appetite	48 (18)	2 (1)	46 (17)	2 (1)
Thrombocytopenia	41 (15)	15 (6)	53 (20)	25 (9)
Fatigue	48 (18)	4 (2)	45 (17)	3 (1)
Vomiting	39 (15)	0	44 (17)	3 (1)

Event	Durvalumab Plus Etoposide (N=265), No. of Patients (%)		Etoposide (N=266), No. of Patients (%)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Asthenia	40 (15)	5 (2)	40 (15)	3 (1)
Leucopenia	40 (15)	17 (6)	32 (12)	14 (5)
Dyspnea	31 (12)	5 (2)	28 (11)	3 (1)
Neutrophil Count Decreased	26 (10)	17 (6)	31 (12)	17 (6)
Diarrhea	26 (10)	3 (1)	30 (11)	3 (1)
Cough	33 (12)	2 (1)	18 (7)	0
Hyponatremia	26 (10)	10 (4)	12 (5)	7 (3)
Febrile Neutropenia	17 (6)	14 (5)	17 (6)	17 (6)
White Blood Cell Count Decreased	14 (5)	4 (2)	17 (6)	6 (2)
Platelet Count Decreased	16 (6)	4 (2)	14 (5)	6 (2)
Pneumonia	11 (4)	5 (2)	18 (7)	9 (3)
Hypertension	15 (6)	8 (3)	7 (3)	1 (<1)
Lipase Increased	12 (5)	9 (3)	7 (3)	4 (2)
Amylase Increased	11 (4)	6 (2)	2 (1)	1 (<1)

Paz-Ares L, et al. *N Engl J Med.* 2019.



Adverse Events Related to the Trial Regimen

Event	Durvalumab Plus Etoposide (N=265), No. of Patients (%)		Etoposide (N=266), No. of Patients (%)	
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Leucopenia	40 (15)	17 (6)	32 (12)	14 (5)
Dyspnea	31 (12)	5 (2)	28 (11)	3 (1)
Neutrophil Count Decreased	26 (10)	17 (6)	31 (12)	17 (6)
Diarrhea	26 (10)	3 (1)	30 (11)	3 (1)
Cough	33 (12)	2 (1)	18 (7)	0
Hyponatremia	26 (10)	10 (4)	12 (5)	7 (3)
Febrile Neutropenia	17 (6)	14 (5)	17 (6)	17 (6)
White Blood Cell Count Decreased	14 (5)	4 (2)	17 (6)	6 (2)
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Any Events With Incidence \geq 10% (Any Grade) or \geq 2% (Grade 3 or 4)				
Neutropenia	111 (42)	64 (24)	124 (47)	88 (33)
Anemia	102 (38)	24 (9)	125 (47)	48 (18)
Nausea	89 (34)	1 (<1)	89 (33)	5 (2)
Alopecia	83 (31)	3 (1)	91 (34)	2 (1)
Constipation	44 (17)	2 (1)	51 (19)	0
Decreased Appetite	48 (18)	2 (1)	46 (17)	2 (1)
Thrombocytopenia	41 (15)	15 (6)	53 (20)	25 (9)
Fatigue	48 (18)	4 (2)	45 (17)	3 (1)
Vomiting	39 (15)	0	44 (17)	3 (1)

Event	Durvalumab Plus Etoposide (N=265), No. of Patients (%)		Etoposide (N=266), No. of Patients (%)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Asthenia	40 (15)	5 (2)	40 (15)	3 (1)
Leucopenia	40 (15)	17 (6)	32 (12)	14 (5)
Dyspnea	31 (12)	5 (2)	28 (11)	3 (1)
Neutrophil Count Decreased	26 (10)	17 (6)	31 (12)	17 (6)
Diarrhea	26 (10)	3 (1)	30 (11)	3 (1)
Cough	33 (12)	2 (1)	18 (7)	0
Hyponatremia	26 (10)	10 (4)	12 (5)	7 (3)
Febrile Neutropenia	17 (6)	14 (5)	17 (6)	17 (6)
White Blood Cell Count Decreased	14 (5)	4 (2)	17 (6)	6 (2)
Platelet Count Decreased	16 (6)	4 (2)	14 (5)	6 (2)
Pneumonia	11 (4)	5 (2)	18 (7)	9 (3)
Hypertension	15 (6)	8 (3)	7 (3)	1 (<1)
Lipase Increased	12 (5)	9 (3)	7 (3)	4 (2)
Amylase Increased	11 (4)	6 (2)	2 (1)	1 (<1)

Paz-Ares L, et al. *N Engl J Med.* 2019.



Adverse Events Related to the Trial Regimen

Event	Durvalumab Plus Etoposide (N=265), No. of Patients (%)		Etoposide (N=266), No. of Patients (%)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Any Adverse Event	260 (98)	163 (62)	258 (97)	166 (62)
Any Serious Event	82 (31)	57 (22)	96 (36)	70 (26)
Any Event Leading to Discontinuation	25 (9)	7 (3)	25 (9)	7 (3)
Any Event Leading to Death	13 (5)	--	15 (6)	--
Any Events With Incidence \geq 10% (Any Grade) or \geq 2% (Grade 3 or 4)				
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Paz-Ares L, et al. *N Engl J Med.* 2019.



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Platelet Count Decreased	16 (6)	4 (2)	14 (5)	6 (2)
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Paz-Ares L, et al. *N Engl J Med.* 2019.



Tarlatamab Versus Chemotherapy as Second-Line Treatment for Small Cell Lung Cancer (SCLC): Primary Analysis of the Phase 3 DeLLphi-304 Study

Charles M. **Rudin**, Giannis S. **Mountzios**, Longhua **Sun**, Byoung **Chul Cho**, Umut **Demirci**, Sofia **Baka**, Mahmut **Gumus**, Antonio **Lugini**, Tudor-Eliade **Ciuleanu**, Myung-Ju **Ahn**, Pedro **Rocha**, Bo **Zhu**, Fiona **Blackhall**, Tatsuya **Yoshida**, Taofeek K. **Owonikoko**, Luis **Paz-Ares**, Shuang **Huang**, Diana **Gauto**, Gonzalo **Recondo**, Martin **Schuler**

J Clin Oncol 43, 2025 (suppl 17; abstr LBA8008)



DeLLphi-304 Study

Key Inclusion Criteria

- Histologically or cytologically **confirmed SCLC**
- **Progression after 1L platinum-based chemotherapy +/- anti-PD-(L)1**
- **ECOG PS 0 or 1**
- **Asymptomatic**, treated or untreated **brain metastases**

Randomization Stratified By

- **Prior anti-PD-(L)1 exposure** (yes/no)
- **CTFI** (<90 days vs ≥90 to 180 days vs ≤180 days)
- **Presence of** (previous/current) **brain metastases** (yes/no)
- **Intended chemotherapy** (topotecan/amrubicin vs lurbinectedin)



Tarlatamab (n = 254)

Chemotherapy* (n = 255)

Topotecan (n = 185); Lurbinectedin (n = 47);
Amrubicin (n = 23)

Primary Endpoint:
Overall Survival

Key Secondary Endpoints:
Progression-Free Survival,
Patient-Reported Outcomes

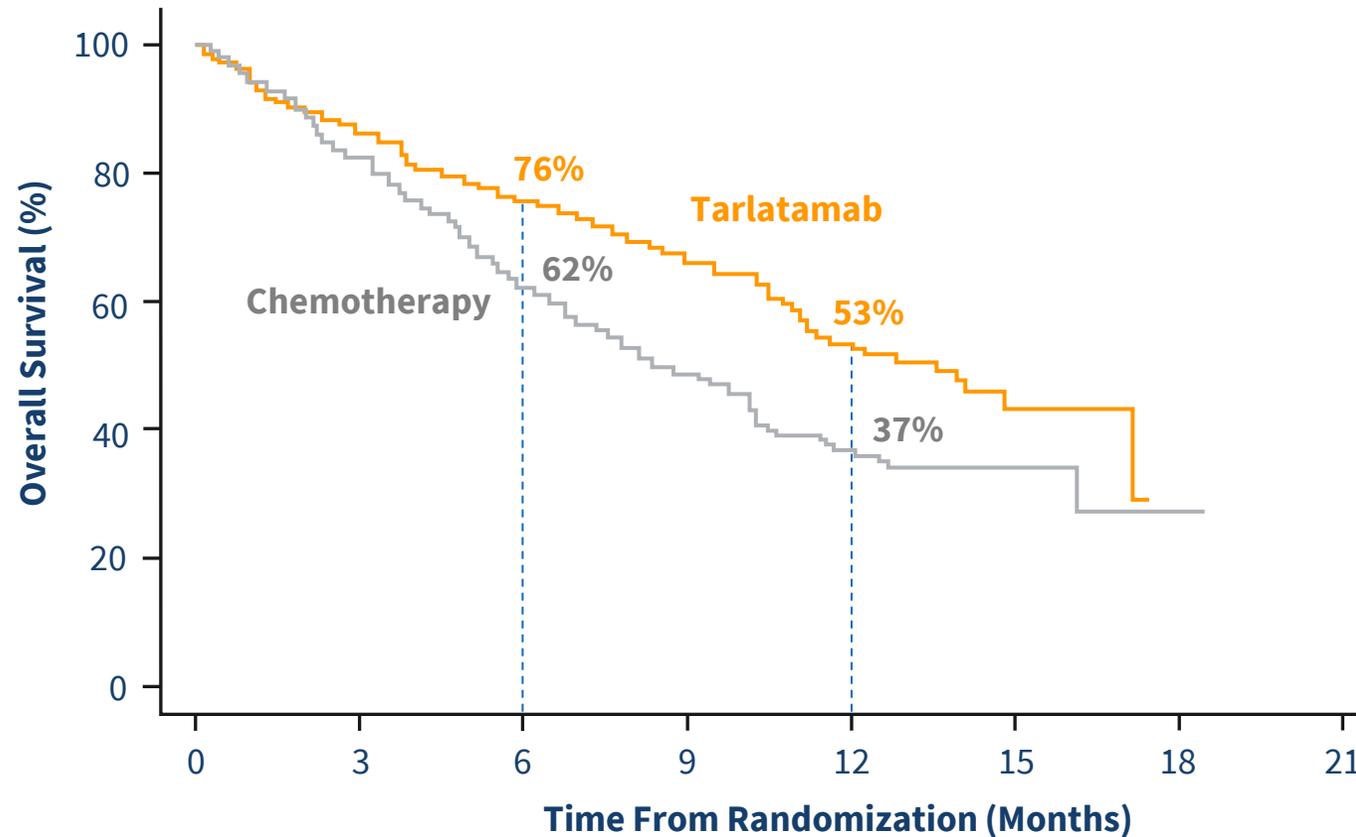
Other Secondary Endpoints:
Objective Response Disease Control,
Duration of Response, Safety

*Topotecan was used in all countries except Japan, lurbinectedin in Australia, Canada, Republic of Korea, Singapore and the United States, and amrubicin in Japan. Abbreviations: 1L = first-line; ECOG PS = Eastern Cooperative Oncology Group performance status; PD-(L)1 = programmed death (ligand)-1; R = randomization.

Rudin C, et al. *J Clin Oncol*. 2025.



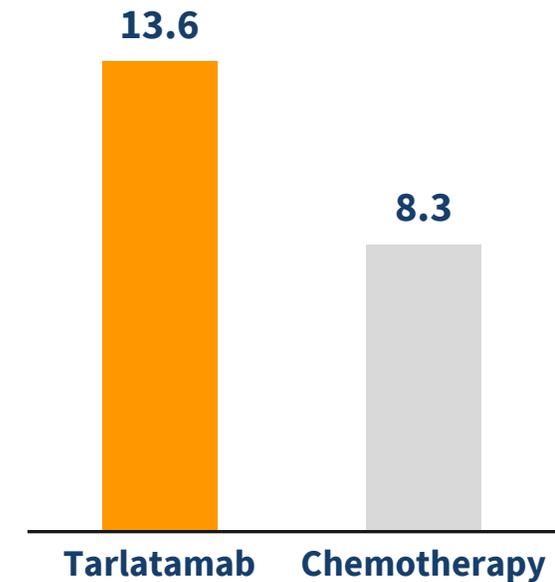
DeLLphi-304: Overall Survival



Median Overall Survival (Months)

HR 0.60 (95% CI 0.47-0.77)

$P < 0.001$



Rudin C, et al. *J Clin Oncol*. 2025.



DeLLphi-304: Hematological Adverse Events

Neutropenia

Grade 1: $\geq 1,500$ to $< 2,000/\mu\text{L}$

Grade 2: $\geq 1,000$ to $< 1,500/\mu\text{L}$

Grade 3: ≥ 500 to $< 1,000/\mu\text{L}$

Grade 4: $< 500/\mu\text{L}$

Anemia

Grade 1: Hgb $< \text{LLN}$ ≥ 10.0 g/dL

Grade 2: Hgb 8.0 to < 10.0 g/dL

Grade 3: Hgb 6.5 to < 8.0 g/dL

Grade 4: Hgb < 6.5 g/dL

Thrombocytopenia

Grade 1: $< \text{LLN}$ to $75\text{k}/\mu\text{L}$

Grade 2: $< 75\text{k}$ to $50\text{k}/\mu\text{L}$

Grade 3: $< 50\text{k}$ to $25\text{k}/\mu\text{L}$

Grade 4: $< 25\text{k}/\mu\text{L}$

Event	Tarlatamab, N = 252 No. of Patients (%)	Etoposide (N=266), N = 244 No. of Patients (%)
Adverse Event in $\geq 10\%$ of Either Group (Any Grade)		
Neutrophil Count Decrease	20 (8)	42 (17)
Febrile Neutropenia	5 (2)	28 (11)
Leukopenia	24 (10)	54 (22)
Platelet Count Decrease	10 (4)	44 (18)
Thrombocytopenia	14 (6)	62 (25)
Neutropenia	27 (11)	76 (31)
Anemia	78 (31)	156 (64)
Adverse Event in $\geq 5\%$ of Either Group (Grade 3 or 4)		
Hyponatremia	12 (5)	13 (5)
Pneumonia	14 (6)	20 (8)
Fatigue	9 (4)	17 (7)
Neutrophil Count Decrease	10 (4)	28 (11)
Platelet Count Decrease	1 (< 1)	20 (8)
Febrile Neutropenia	5 (2)	28 (11)
Thrombocytopenia	2 (1)	28 (11)
Leukopenia	4 (2)	34 (14)
Neutropenia	15 (6)	57 (23)
Anemia	11 (4)	70 (29)

*Prophylactic growth factor (G-CSF) was permitted based on investigator's discretion. (%) patients receiving G-CSF has not been disclosed.

Mountzios G, et al. *N Engl J Med.* 2025.



DeLLphi-304: Hematological Adverse Events

Neutropenia

Grade 1: $\geq 1,500$ to $< 2,000/\mu\text{L}$

Grade 2: $\geq 1,000$ to $< 1,500/\mu\text{L}$

Grade 3: ≥ 500 to $< 1,000/\mu\text{L}$

Grade 4: $< 500/\mu\text{L}$

Anemia

Grade 1: Hgb $< \text{LLN}$ ≥ 10.0 g/dL

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Thrombocytopenia

Grade 1: $< \text{LLN}$ to $75\text{k}/\mu\text{L}$

Grade 2: $< 75\text{k}$ to $50\text{k}/\mu\text{L}$

Grade 3: $< 50\text{k}$ to $25\text{k}/\mu\text{L}$

Grade 4: $< 25\text{k}/\mu\text{L}$

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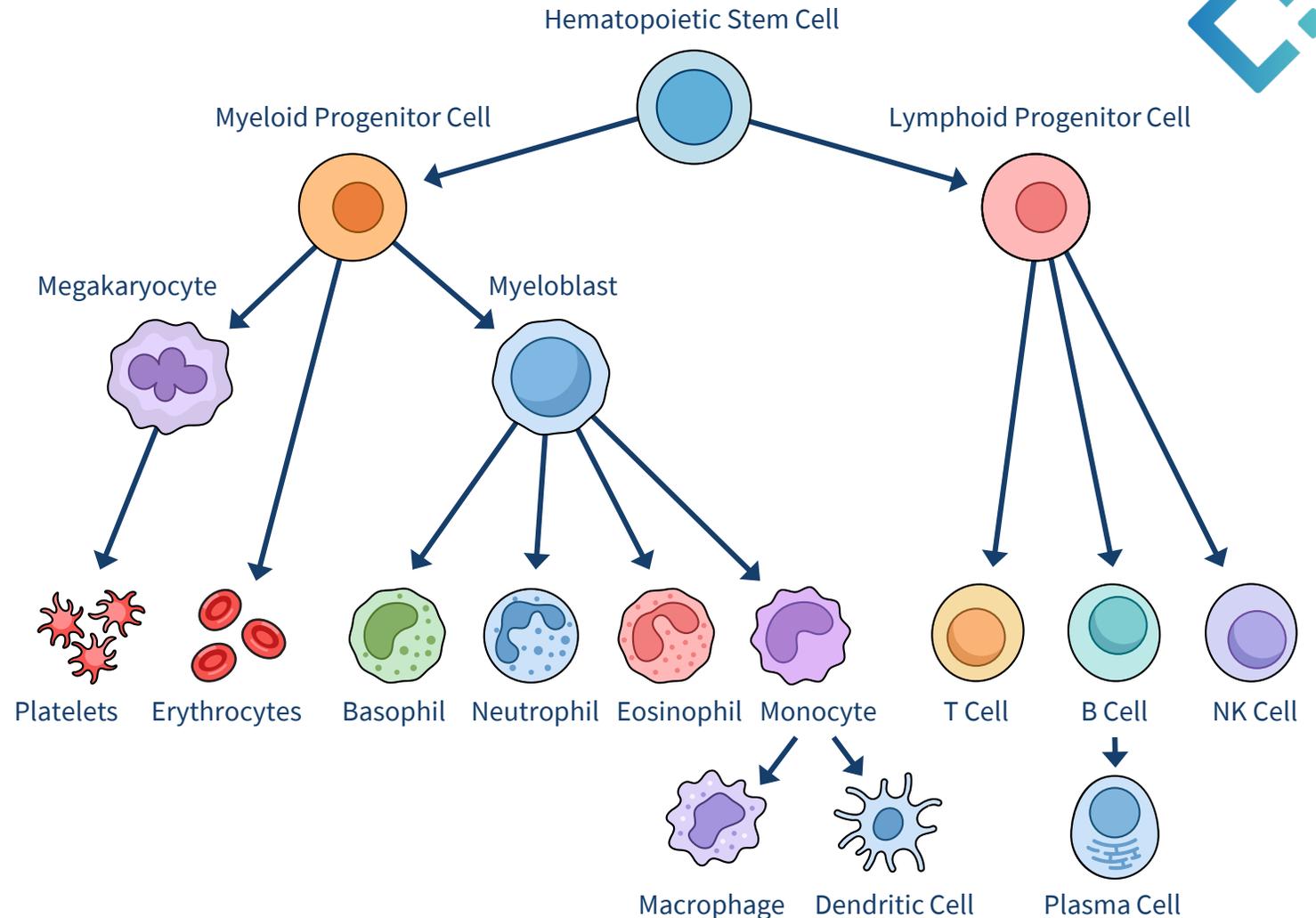
Supporting the Bone Marrow in ES-SCLC Management

Expert Analysis of Myeloprotective Best Practices



Hematopoiesis

- HSCs divide to generate multipotent progenitors.
- Progenitors divide to progressively more differentiated cells.
- Eventually, they give origin to mature cells, which include:
 - Red blood cells (RBCs)
 - White blood cells (WBCs) of the immune system
 - Platelet-producing megakaryocytes
- **Blood cell maturation is stimulated by specific hematopoietic growth factors.**



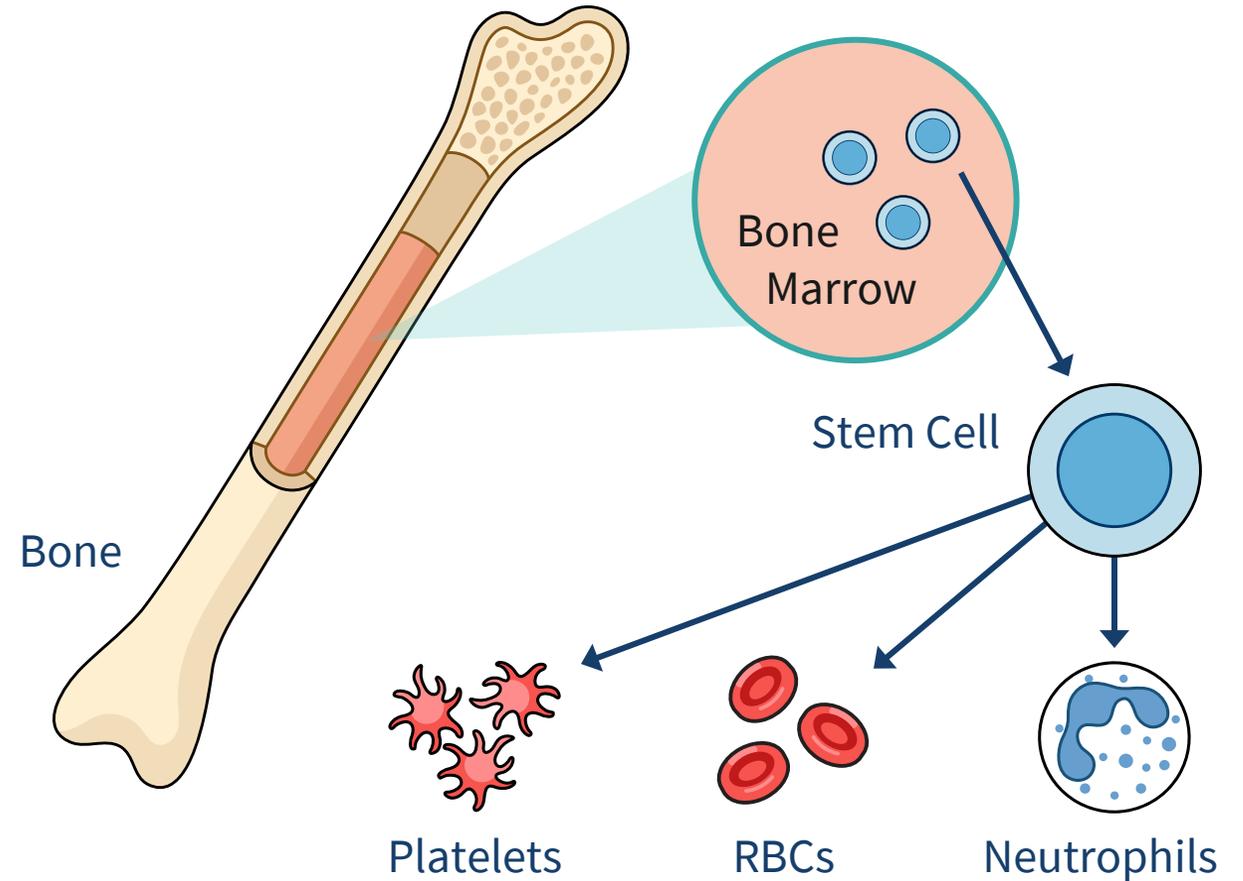
Shier D, Butler J, Lewis R. *Blood* (Ch 14). In: Hole's Human Anatomy & Physiology. 14th Ed. McGraw-Hill Education; 2016.; White blood cell. NCI Dictionary of Cancer Terms; Hematopoietic growth factor. NCI Dictionary of Cancer Terms.



Types of Cytopenia



- The type of cytopenia depends on which blood cell counts are low.
- When **all 3 peripheral blood cell lines are low**, the corresponding cytopenia is called **pancytopenia**.



Bagheri Z, et al. *J Comp Eff Res*. 2020; Neutrophil. National Cancer Institute. NCI Dictionary of Cancer Terms; Hart L, et al. *Cancer Med*. 2023; Epstein R, et al. *Adv Ther*. 2020; NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025.

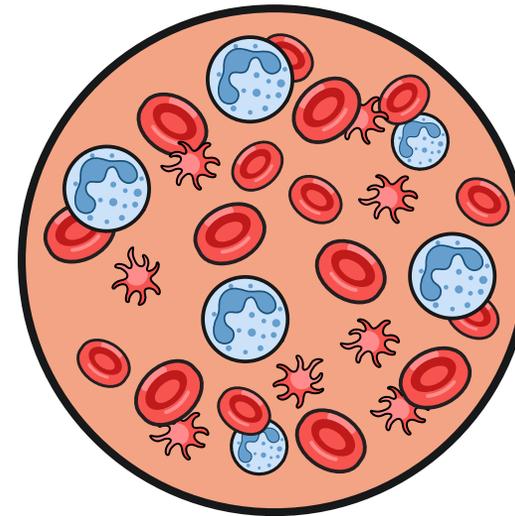


Neutropenia

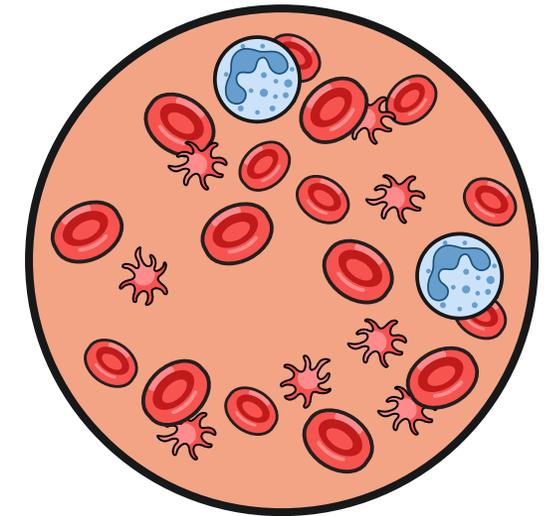


- Neutropenia is caused by a **low count of neutrophils** (the most abundant type of WBCs).
- Neutropenia is defined by a count <1500 cells/ μL .
 - If the count is <500 cells/ μL , neutropenia is **severe**.
- WBCs are key players in the immune system.
 - **Neutrophils are the first WBCs to arrive at an infection site.**
- Neutropenia can increase a person's risk of infection.

Blood Cells Under Microscope



Normal

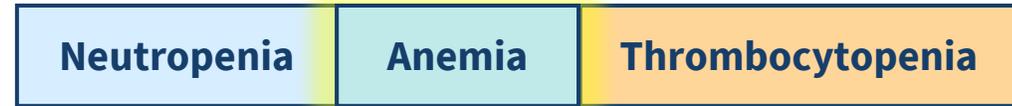


Neutropenia

Shier D, Butler J, Lewis R. *Blood* (Ch 14). In: Hole's Human Anatomy & Physiology. 14th Ed. McGraw-Hill Education; 2016; Bagheri Z, et al. *J Comp Eff Res*. 2020; Neutropenia (low white blood cell counts). American Cancer Society; NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025.

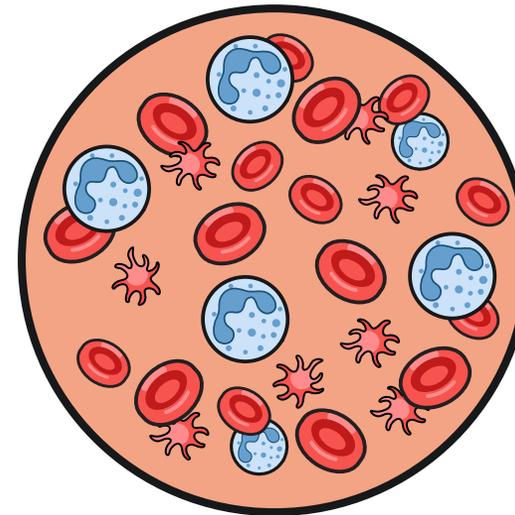


Anemia

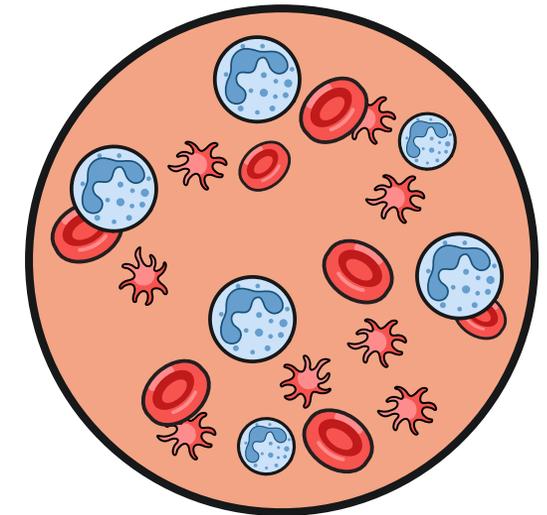


- In people with anemia, the number of red blood cells (erythrocytes) is below normal.
- Anemia is defined as a hemoglobin (Hb or Hgb) concentration:
 - <12 g/dL for females
 - <13 g/dL for males
- Erythrocytes are the cells that supply oxygen to tissues and cells throughout the body.
- Anemia reduces the amount of oxygen the body receives.

Blood Cells Under Microscope



Normal



Anemia

Shier D, Butler J, Lewis R. *Blood* (Ch 14). In: Hole's Human Anatomy & Physiology. 14th Ed. McGraw-Hill Education; 2016; Bagheri Z, et al. *J Comp Eff Res*. 2020; NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025; Rodgers GM. *Expert Rev Hematol*. 2024.

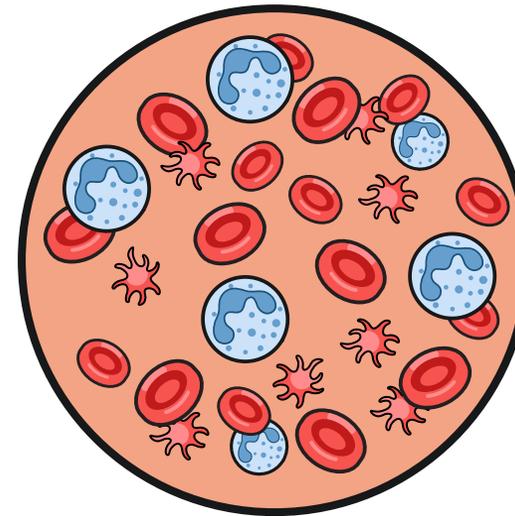


Thrombocytopenia

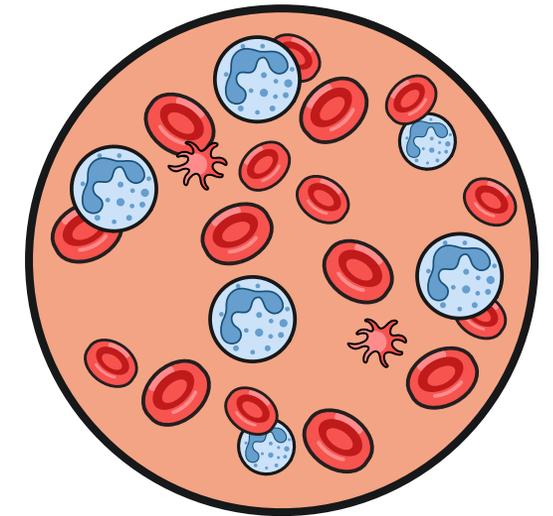
Neutropenia	Anemia	Thrombocytopenia
-------------	--------	------------------

- Thrombocytopenia describes low platelet (thrombocytes) levels.
 - Thrombocytopenia is defined by a count $<150,000$ platelets/ μL of blood.
- Platelets are needed for blood to clot and help repair damaged blood vessels.
 - In patients with thrombocytopenia, the blood clotting mechanism is defective, leading to an elevated risk of bleeding.

Blood Cells Under Microscope



Normal



Thrombocytopenia

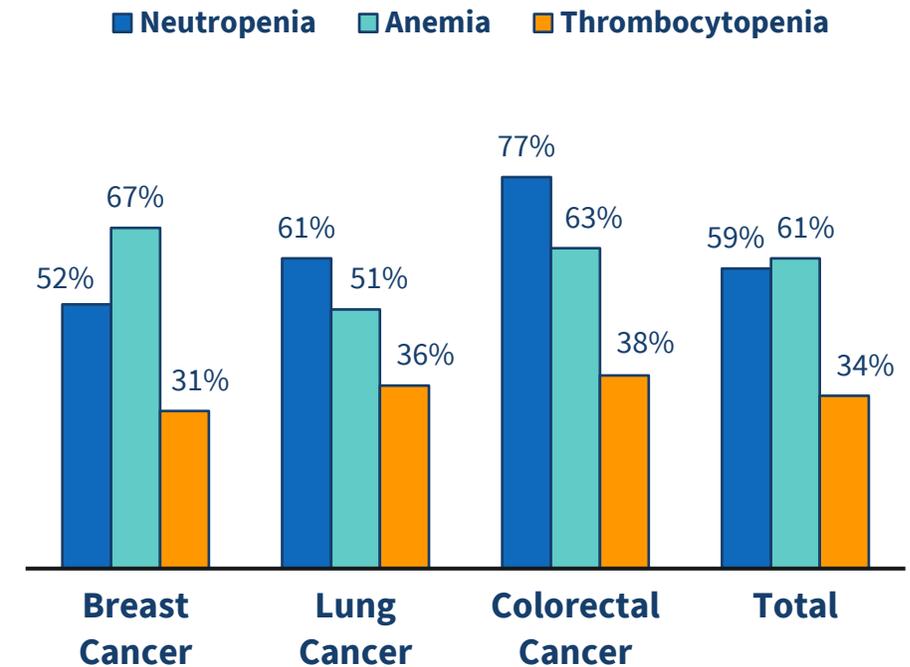
Shier D, Butler J, Lewis R. *Blood* (Ch 14). In: Hole's Human Anatomy & Physiology. 14th Ed. McGraw-Hill Education; 2016; Bagheri Z, et al. *J Comp Eff Res*. 2020; NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025; Schiffer C, et al. *J Clin Oncol*. 2018.



Real-World Management of Chemotherapy-Induced Myelosuppression

- Online survey of 301 participants who had received chemotherapy in the last 12 months and experienced at least one episode of myelosuppression
- Most patients (88%) considered myelosuppression to have a moderate or major impact on quality of life
 - Impact was significantly higher in patients <50 years compared with those \geq 50 years of age

Patient Report of Myelosuppression Diagnosis



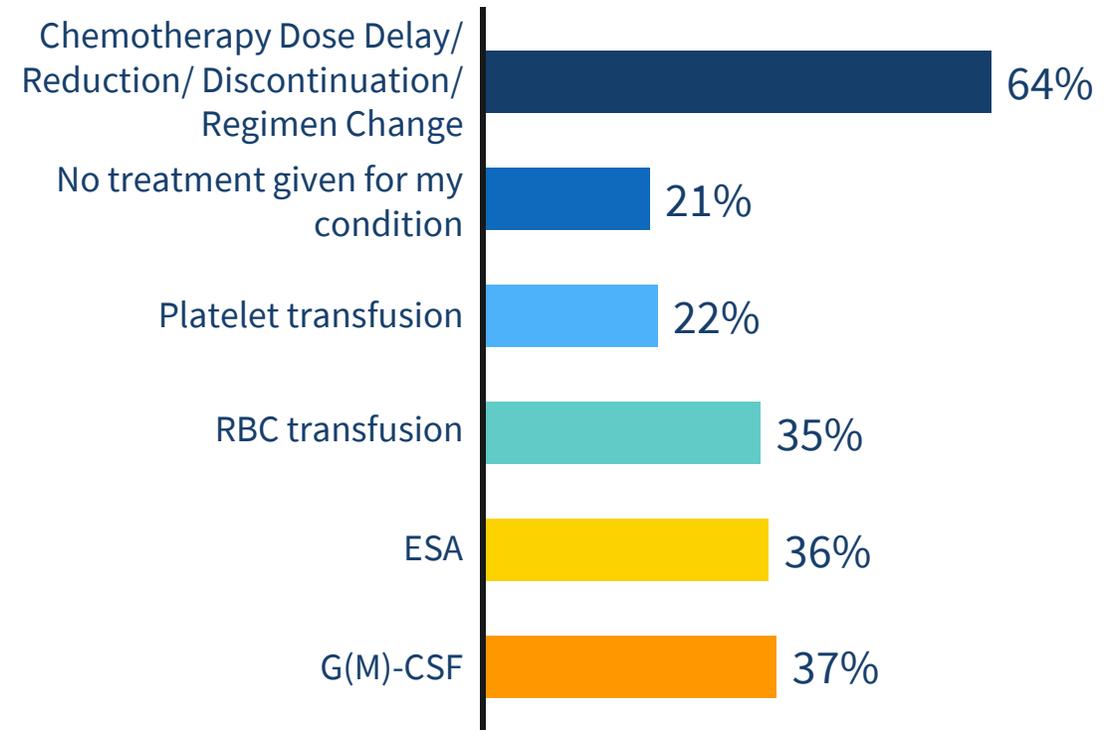
Epstein R, et al. *Patient Prefer Adherence*. 2021.



Real-World Management of Chemotherapy-Induced Myelosuppression

- As most patients reported being diagnosed with neutropenia or anemia, it is not surprising that G(M)-CSF, ESAs, and RBC transfusions were the most common supportive care measures, each being reported in roughly 1/3 of patients

Patient Reported Intervention of Myelosuppression

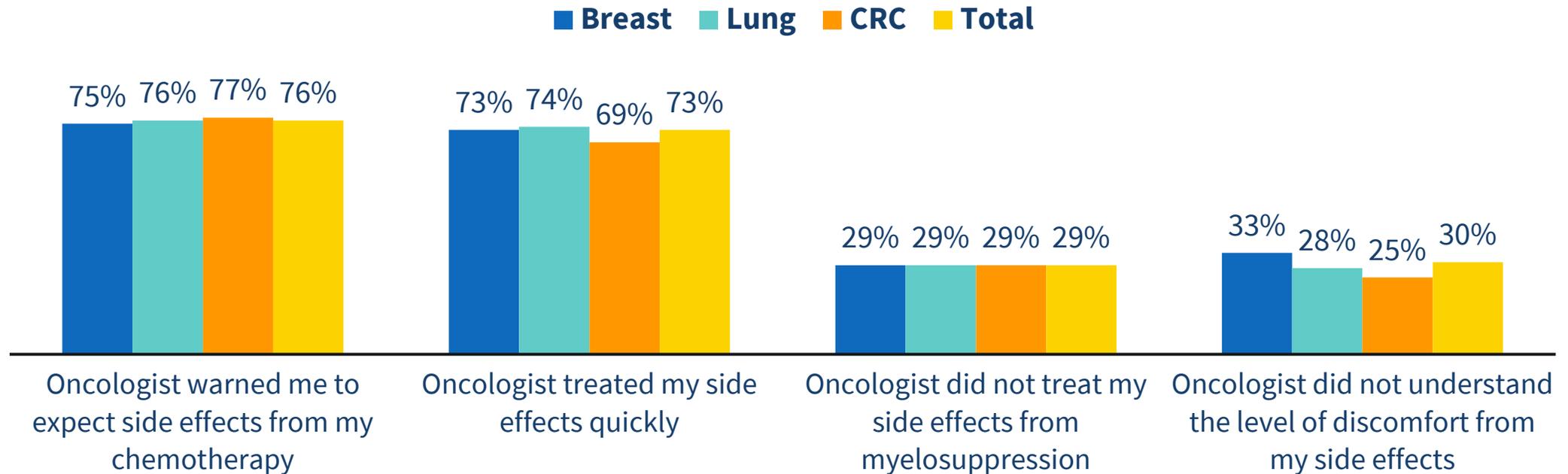


Epstein R, et al. *Patient Prefer Adherence*. 2021.



Real-World Management of Chemotherapy-Induced Myelosuppression

Patient-Reported Side Effect Management

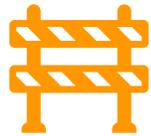


Epstein R, et al. *Patient Prefer Adherence*. 2021.



Current Management Strategies of Hematopoietic Toxicities

Prophylactic Cell Lineage Intervention



Treatment Cycle Restriction (6 → 4)



Dose Adjustments for Chemotherapy



Trilaciclib
(CDK 4/6 Inhibitor)



Interphasing of IO
(Tarlatabamab)

Reactive Cell Lineage Intervention



Anemia:
ESA, Blood Transfusions



Neutropenia/Leukopenia:
G-CSF/GM-CSF
(Primary/Secondary Prevention)



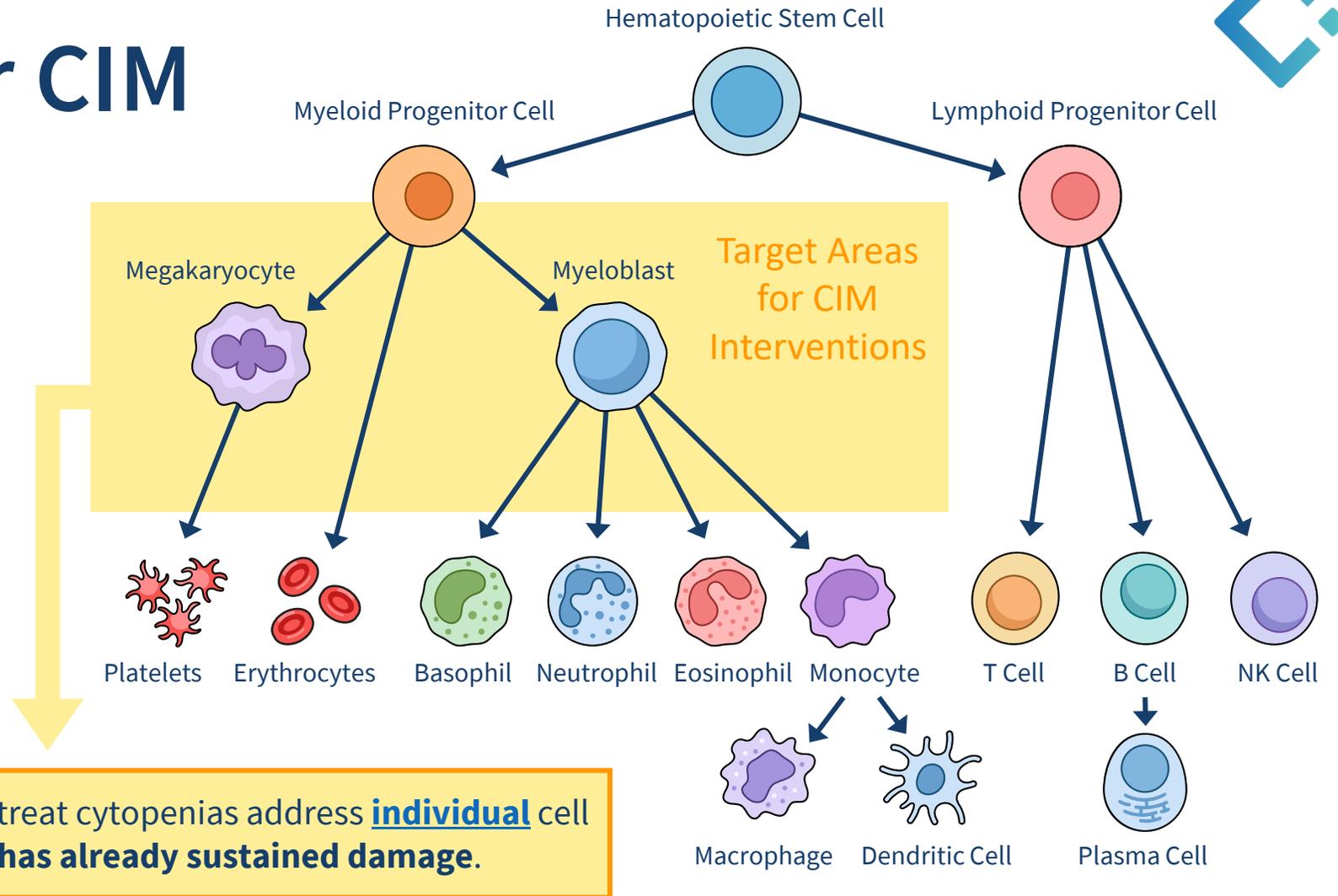
Thrombocytopenia:
Permissive Observation, Platelet Transfusions, and TPOs (*not approved*)

NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025; NCCN Clinical Practice Guidelines: Small Cell Lung Cancer. Version 2.2026; Kalemkerian G, et al. *J Clin Oncol*. 2025.



Therapies for CIM

- Supportive care interventions for CIM include:
 - Growth factors
 - G-CSFs for neutropenia
 - ESAs for anemia
 - Blood transfusions for
 - Anemia
 - Thrombocytopenia

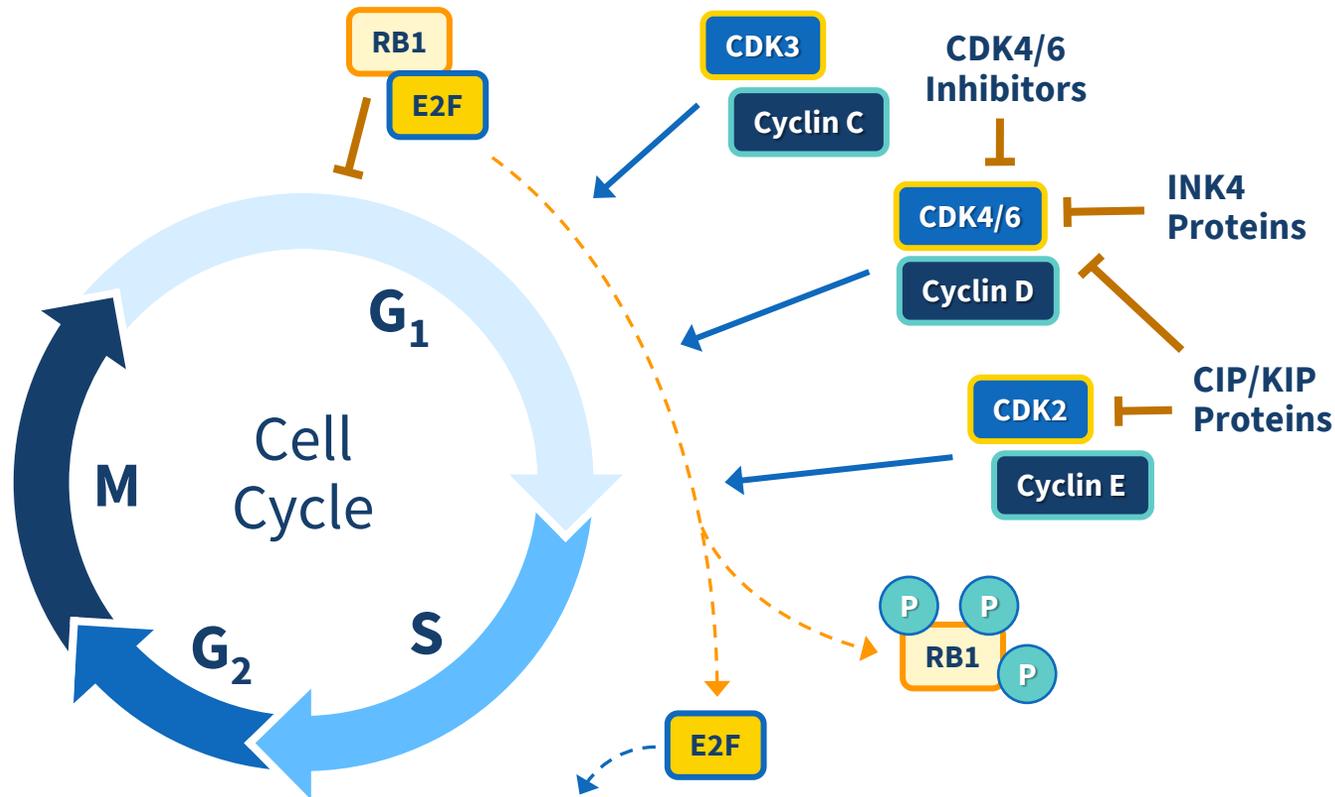


KEY POINT: The interventions to treat cytopenias address individual cell lineages after the bone marrow has already sustained damage.

Hart L, et al. *Cancer Med.* 2023; Crawford J, et al. *Future Oncol.* 2024; Granulocyte colony-stimulating factor. National Cancer Institute. NCI Dictionary of Cancer Terms; Erythropoiesis. National Cancer Institute. NCI Dictionary of Cancer Terms; NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025; Goldschmidt J, et al. *Future Oncol.* 2022.



SCLC & CDK4/6 Inhibition



1. RB1 inhibits cell cycle transition from G₁/S and G₂/M phase transition points for DNA repair.
2. CDK4/6 is involved in cell cycle propagation in hematopoietic stem cells.
3. CDK4/6 de-activates RB1 protein and advances cell cycle via phosphorylation of RB1.
4. Inhibition of CDK4/6 leads to cell arrest of proliferation in the HPSC compartment.
5. Prolonged exposure leads to cytopenias; short term exposure can confer myeloprotection.
6. In SCLC, >90% of tumors = Rb1 deficient, allowing for ongoing tumor cell proliferation unaffected by CDK4/6.

Hart L, et al. *Cancer Med.* 2023; Crawford J, et al. *Future Oncol.* 2024; Roberts P, et al. *Mol Cancer Ther.* 2020; Weiss J, et al. *Ann Oncol.* 2019; Weiss J, et al. *Clin Lung Cancer.* 2021; Daniel D, et al. *Int J Cancer.* 2021.



Myeloprotection With Trilaciclib

Study 1

Pivotal

(G1T28-05; NCT03041311)

Newly diagnosed

ES-SCLC **not previously treated** with chemotherapy

Trilaciclib or placebo prior to E/P/A on days 1-3 of 21-day cycles × 4 cycles, followed by maintenance with a monotherapy

107 Patients:

Trilaciclib n = 54, Placebo n = 53

Stratified by ECOG PS (0/1 vs 2) and presence of brain metastases

Myeloprotection, safety, tolerability, PK, antitumor efficacy

Study 2

Exploratory, proof-of-concept, supportive

(G1T28-02; NCT02499770)

Newly diagnosed

ES-SCLC **not previously treated** with chemotherapy

Trilaciclib or placebo prior to E/P on days 1-3 of 21-day cycles, until discontinuation from PI discretion

77 Patients:

Trilaciclib n = 39, Placebo n = 38

Stratified by ECOG PS (0/1 vs 2)

Part 1: DLTs, RP2D, safety, tolerability

Part 2: Myeloprotection, safety, tolerability, PK, antitumor efficacy

Study 3

Exploratory, supportive

(G1T28-03; NCT02514447)

ES-SCLC **previously treated** with chemotherapy

Trilaciclib or placebo prior to topotecan on days 1-5 of 21-day cycles, until disease progression or unacceptable toxicity

61 Patients:

Trilaciclib n = 32, Placebo n = 29

Stratified by ECOG PS (0/1 vs 2) and sensitivity to first-line treatment

Part 1: DLTs, RP2D, safety, tolerability

Part 2: Myeloprotection, safety, tolerability, PK, antitumor efficacy

Weiss J, et al. *Clin Lung Cancer*. 2021.



Study 1

Pivotal

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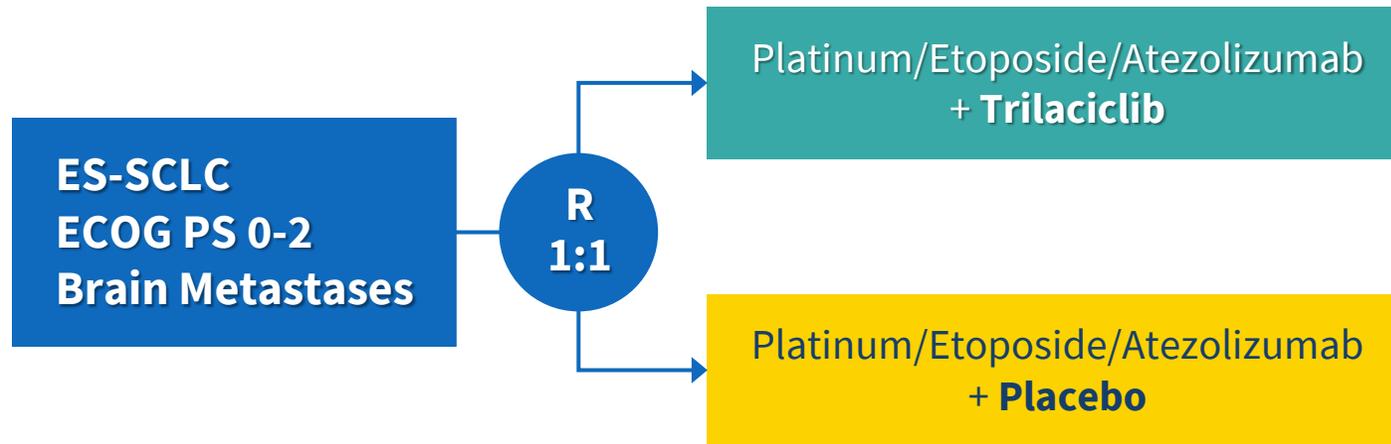
Trilaciclib Prior to Chemotherapy and Atezolizumab in Patients With Newly Diagnosed Extensive-Stage Small Cell Lung Cancer: A Multicentre, Randomised, Double-Blind, Placebo-Controlled Phase II Trial

Davey **Daniel**, Vladimer **Kuchava**, Igor **Bondarenko**, Oleksandr **Ivashchuk**, Sreekanth **Reddy**, Jana **Jaal**, Iveta **Kudaba**, Lowell **Hart**, Amiran **Matitashvili**, Yili **Pritchett**, Shannon R. **Morris**, Jessica A. **Sorrentino**, Joyce M. **Antal**, Jerome **Goldschmidt**

Daniel D, et al. *Int J Cancer*. 2021.



Study 1: Design



Primary Endpoints

- Percent of patients with Grade 4 SN (ANC <500 cells/ μ L)
- Mean number of days with Grade 4 SN in Cycle 1

Secondary Endpoints

- Percent of patients requiring G-CSFs
- Percent of patients requiring RBC transfusions on/after week 5
- Percent of patients requiring platelet transfusions
- Percent of patients with Grades 3 or 4 hematologic laboratory abnormalities
- Percent of patients requiring ESAs
- All-cause chemotherapy dose reductions
- Safety and tolerability

Daniel D, et al. *Int J Cancer*. 2021.



Study 1: Patient Characteristics

Measure		Trilaciclib Prior to E/P/A, N = 54	Placebo Prior to E/P/A, N = 53
Age, years	Median (range)	65 (45-81)	64 (46-83)
	18 to <65, n (%)	27 (50.0)	27 (50.9)
	≥65, n (%)	27 (50)	26 (49)
Sex, n (%)	Male	41 (75.9)	34 (64.2)
	Female	13 (24.1)	19 (35.8)
Race, n (%)	White	53 (98.1)	51 (96.2)
	Black or African American	0	1 (1.9)
	Other	1 (1.9)	1 (1.9)
Region, n (%)	USA	20 (37.0)	22 (41.5)
	Non-USA	34 (63.0)	31 (58.5)
ECOG PS, n (%)	0-1	45 (85.2)	46 (86.8)
	2	8 (14.8)	7 (13.2)
Baseline LDH, n (%)	≤ULN	26 (48.1)	29 (54.7)
	>ULN	25 (46.3)	24 (45.3)
	Missing	3 (5.6)	0
Brain Metastases, n (%)		15 (27.8)	15 (28.3)
Smoking History, n (%)	Never Smoked	4 (7.4)	6 (11.3)
	Former Smokers	26 (48.1)	29 (54.7)
	Current Smokers	23 (42.6)	18 (34.0)
	Missing	1 (1.9)	0
PD-L1 Status, n/n (%)	Negative	13/21 (61.9)	17/27 (63.0)
	Positive	8/21 (38.1)	10/27 (37.0)

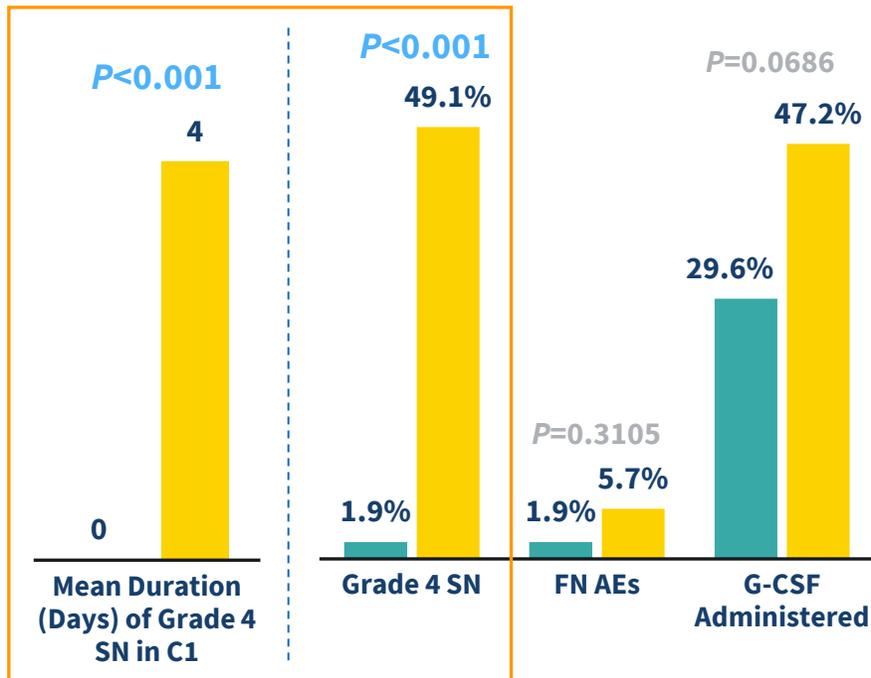
Daniel D, et al. *Int J Cancer*. 2021.



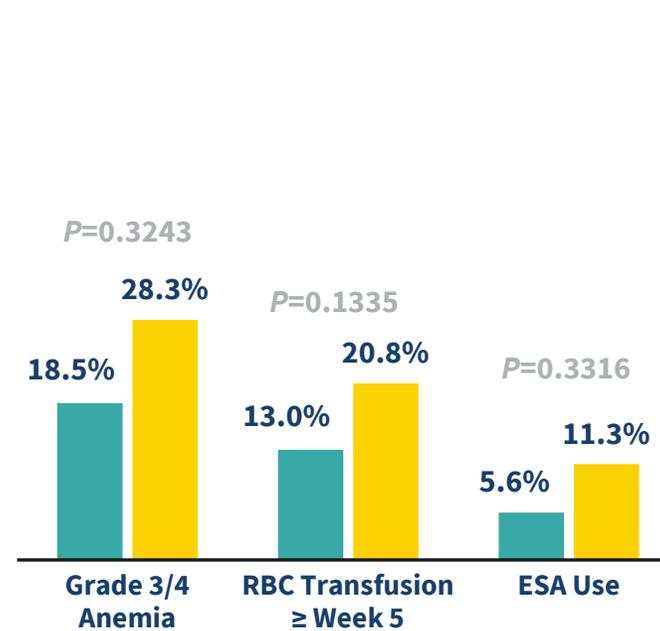
Study 1: Primary/Secondary Outcomes

Primary Endpoints

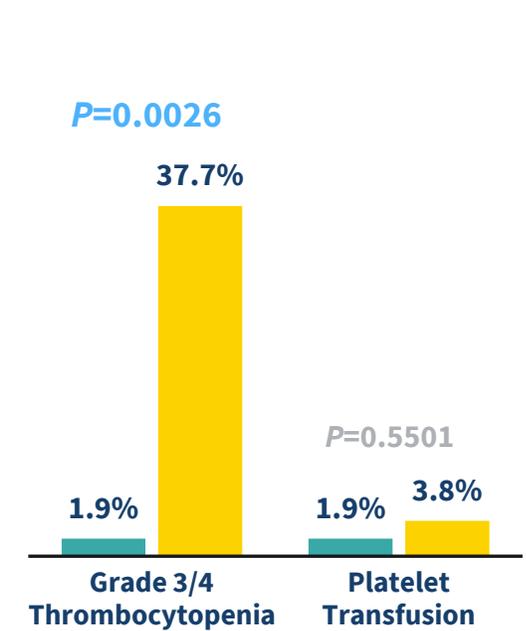
Neutrophil Lineage



RBC Lineage



Platelet Lineage



Summary of myelosuppression endpoints. Data are from the induction phase. P values are raw one-sided or multiplicity-adjusted.

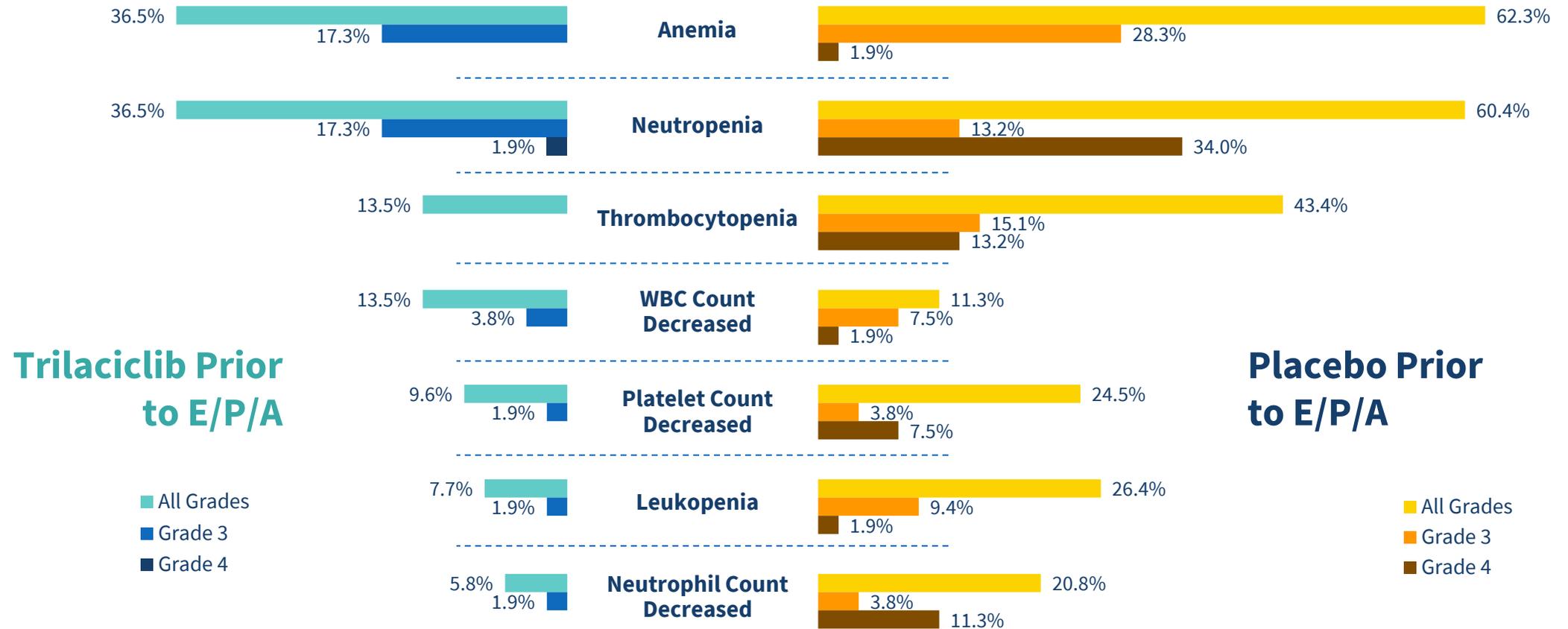
*Multiplicity adjusted P value. Abbreviations: AEs = Adverse Events; C = cycle; E/P/A = Etoposide, Carboplatin and Atezolizumab; ESA = Erythropoiesis-Stimulating Agent; FN = Febrile Neutropenia; G-CSF = Granulocyte Colony-Stimulating Factor; RBC = Red Blood Cell; SN = Severe Neutropenia.

■ Trilaciclib Prior to E/P/A
■ Placebo Prior to E/P/A

Daniel D, et al. *Int J Cancer*. 2021.



Study 1: Hematological AEs Occurring in $\geq 10\%$ of Patients

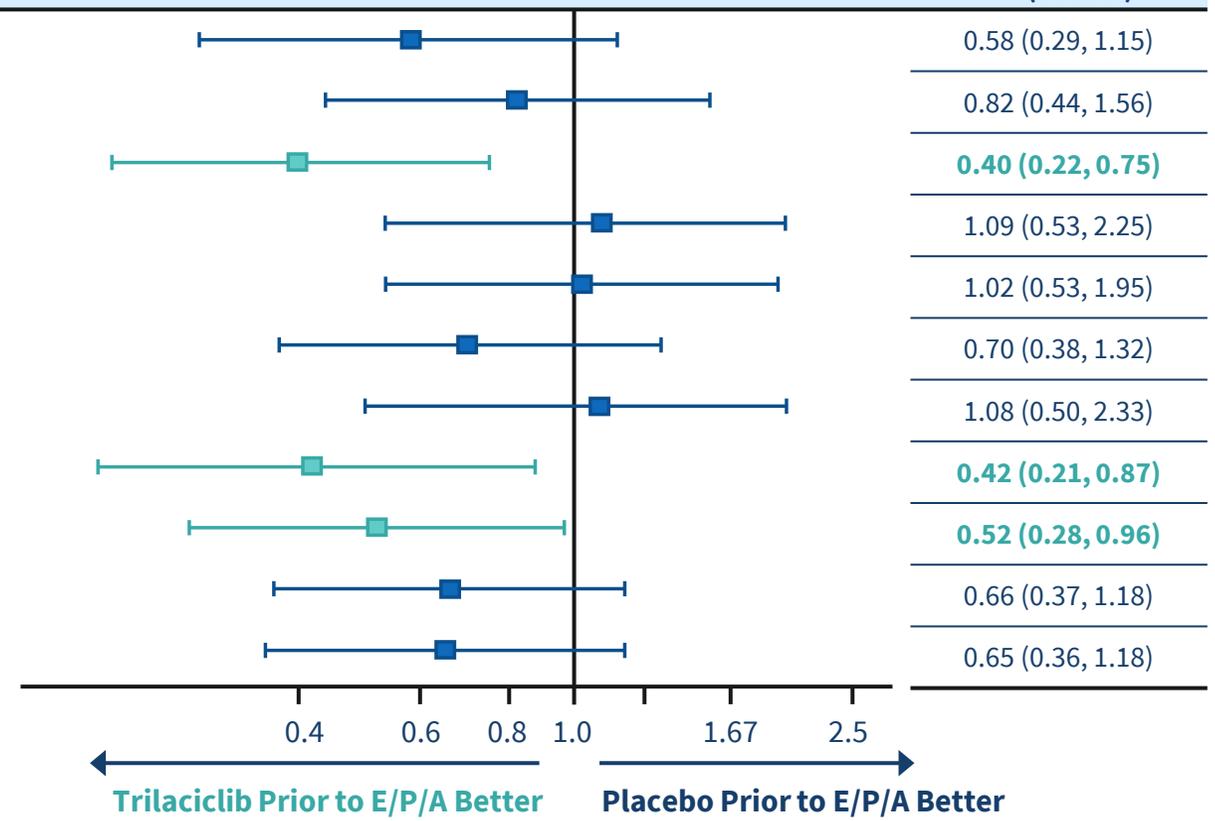


Daniel D, et al. *Int J Cancer*. 2021.



Study 1: Cytopenias & PROs

Domain	Events, n		Median TTD		HR (95% CI)
	Trilaciclib	Placebo	Trilaciclib	Placebo	
FACT-G	13	22	NYR	NYR	0.58 (0.29, 1.15)
PWB	17	22	NYR	NYR	0.82 (0.44, 1.56)
FWB	15	30	8.57	3.53	0.40 (0.22, 0.75)
EWB	15	15	NYR	NYR	1.09 (0.53, 2.25)
SWB	19	18	NYR	NYR	1.02 (0.53, 1.95)
FACT-L	17	23	NYR	7.16	0.70 (0.38, 1.32)
LCS	13	13	NYR	NYR	1.08 (0.50, 2.33)
L-TOI	11	24	NYR	7.95	0.42 (0.21, 0.87)
FACT-An	16	28	NYR	4.17	0.52 (0.28, 0.96)
Fatigue	20	28	7.20	2.60	0.66 (0.37, 1.18)
Anemia TOI	19	27	7.20	3.84	0.65 (0.36, 1.18)

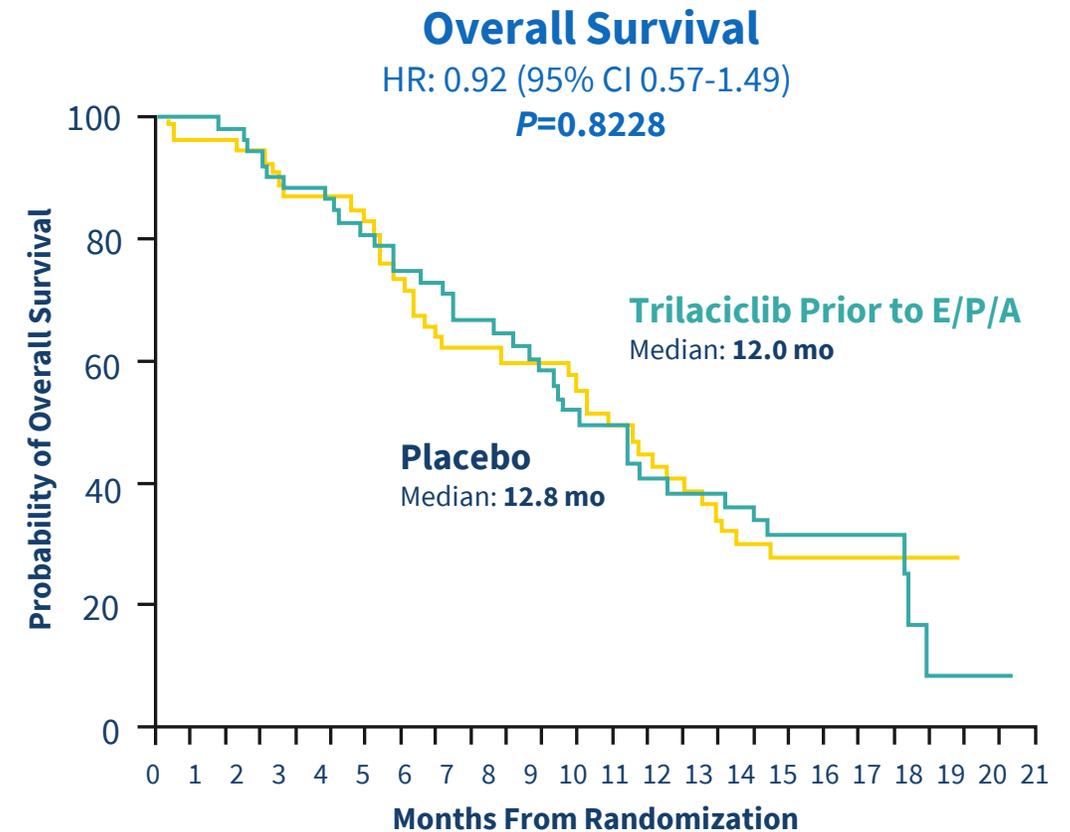
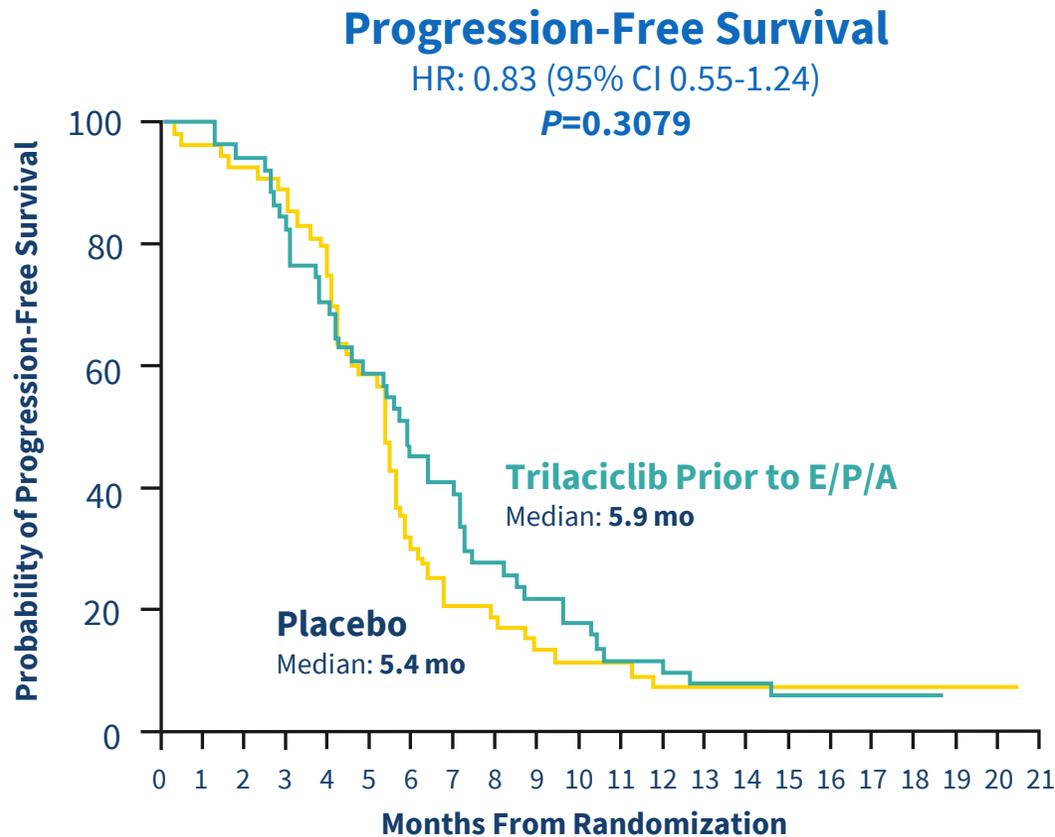


Daniel D, et al. *Int J Cancer*. 2021.

Median time to confirmed deterioration in patient-reported outcomes. Data are from the time of DBL1. DBL1, first database lock (data cutoff: August 17, 2018). Abbreviations: EWB = Emotional Well-Being; FACT-An = Functional Assessment of Cancer Therapy-Anemia; FACT-G = Functional Assessment of Cancer Therapy-General; FACT-L = Functional Assessment of Cancer Therapy-Lung; FWB = Functional Well-Being; LCS = Lung Cancer Subscale; NYR = Not Yet Reached; PWB = Physical Well-Being; SWB = Social Well-Being; TOI = Trial Outcome Index; TTD = Time to Deterioration.



Study 1: Survival Outcomes



Daniel D, et al. *Int J Cancer*. 2021.

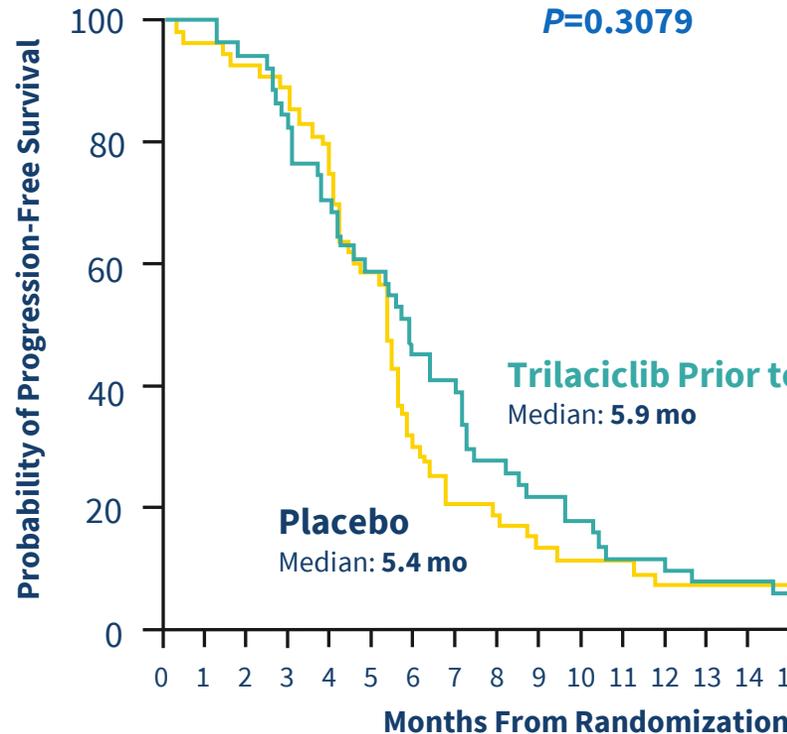


Study 1: Survival Outcomes

Progression-Free Survival

HR: 0.83 (95% CI 0.55-1.24)

P=0.3079



Overall Survival

HR: 0.92 (95% CI 0.57-1.49)

P=0.8228

Study 2

Exploratory, proof-of-concept, supportive

(G1T28-02; NCT02499770)

Newly diagnosed

ES-SCLC **not previously treated** with chemotherapy

Trilaciclib or placebo prior to E/P on days 1-3 of 21-day cycles, until discontinuation from PI discretion

77 Patients:

Trilaciclib n = 39, Placebo n = 38

Stratified by ECOG PS (0/1 vs 2)

Part 1: DLTs, RP2D, safety, tolerability

Part 2: Myeloprotection, safety, tolerability, PK, antitumor efficacy

Similar results were seen with Study 2 without immunotherapy without significant observed differences.

Weiss J, et al. *Clin Lung Cancer*. 2021; Daniel D, et al. *Int J Cancer*. 2021.



Study 3

Exploratory, supportive
(G1T28-03; NCT02514447)

ES-SCLC **previously treated** with
chemotherapy

Trilaciclib or placebo prior to topotecan
on days 1-5 of 21-day cycles, until disease
progression or unacceptable toxicity

61 Patients:

Trilaciclib n = 32, Placebo n = 29

Stratified by ECOG PS (0/1 vs 2) and
sensitivity to first-line treatment

Part 1: DLTs, RP2D, safety, tolerability

Part 2: Myeloprotection, safety,
tolerability, PK, antitumor efficacy

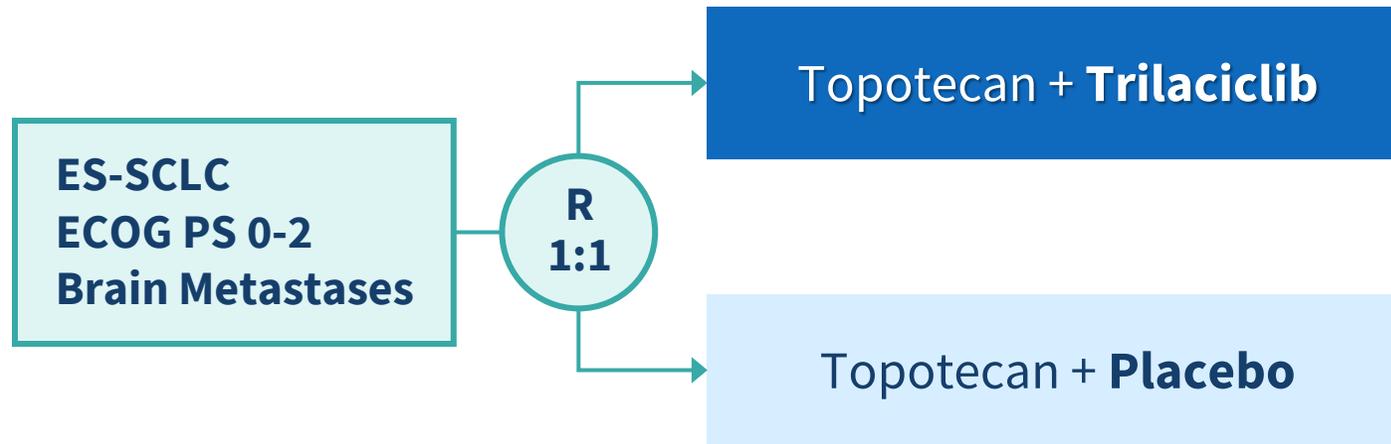
Myelopreservation With Trilaciclib in Patients Receiving Topotecan for Small Cell Lung Cancer: Results From a Randomized, Double-Blind, Placebo-Controlled Phase II Study

Lowell L. **Hart**, Renata **Ferrarotto**, Zoran G. **Andric**, J Thaddeus **Beck**, Janakiraman **Subramanian**, Davorin Z. **Radosavljevic**, Bojan **Zaric**, Wahid T. **Hanna**, Raid **Aljumaily**, Taofeek K. **Owonikoko**, Didier **Verhoeven**, Jie **Xiao**, Shannon R. **Morris**, Joyce M. **Antal**, Maen A. **Hussein**

Weiss J, et al. *Clin Lung Cancer*. 2021; Hart L, et al. *Adv Ther*. 2021.



Study 3: Design



Primary Endpoints

- Percent of patients with Grade 4 SN (ANC <500 cells/ μ L)
- Mean number of days with Grade 4 SN in Cycle 1

Secondary Endpoints

- Percent of patients requiring G-CSFs
- Percent of patients requiring RBC transfusions on/after week 5
- Percent of patients requiring platelet transfusions
- Percent of patients with Grades 3 or 4 hematologic laboratory abnormalities
- Percent of patients requiring ESAs
- All-cause chemotherapy dose reductions
- Safety and tolerability

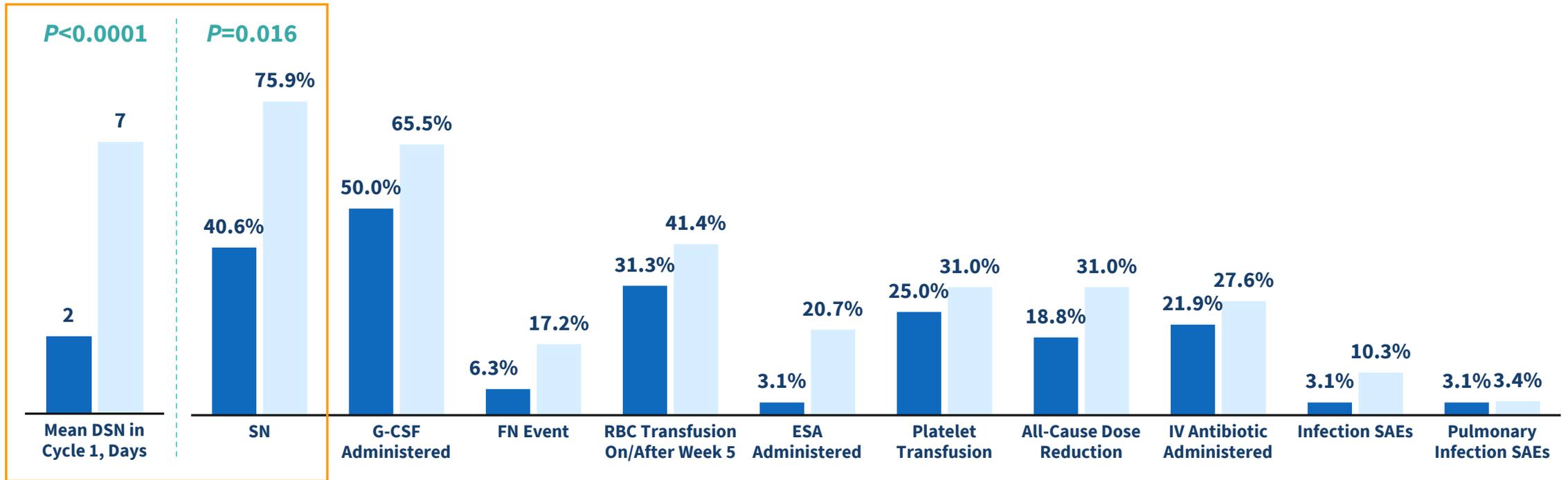
Hart L, et al. *Adv Ther*. 2021.



Study 3: Primary/Secondary Outcomes

Primary Endpoints

■ Trilaciclib Prior to Topotecan ■ Placebo Prior to Topotecan

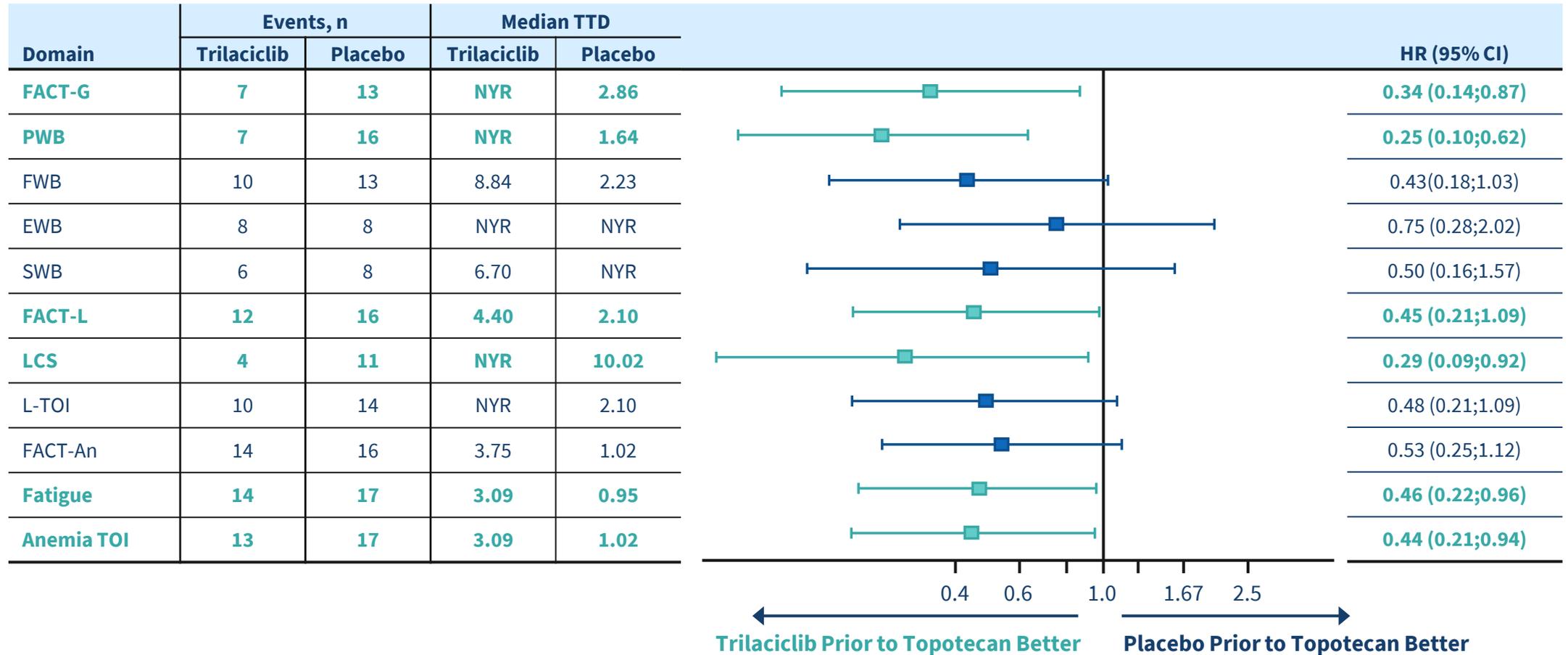


Myelopreservation outcomes. Abbreviations: DSN = Duration of Severe Neutropenia, ESA = Erythropoiesis-Stimulating Agent; FN = Febrile Neutropenia; G-CSF = Granulocyte Colony Stimulating Factor; IV = Intravenous; RBC = Red Blood Cell; SAE = Serious Adverse Event; SN = Severe Neutropenia.

Hart L, et al. *Adv Ther.* 2021.



Study 3: Cytopenias & PROs



Median time to confirmed deterioration in patient-reported outcomes. Abbreviations: EWB = Emotional Well-Being; FACT-An = Functional Assessment of Cancer Therapy-Anemia; FACT-G = Functional Assessment of Cancer Therapy-General; FACT-L = Functional Assessment of Cancer Therapy-Lung; FWB = Functional Well-Being; LCS = Lung Cancer Subscale; NYR = Not Yet Reached; PWB = Physical Well-Being; SWB = Social Well-Being; TOI = Trial Outcome Index; TTD = Time to Deterioration.

Hart L, et al. *Adv Ther.* 2021.



Trilaciclib – FDA Approval

- Initial FDA-approval = February 2021
- Most recent label update = August 2025
- Indicated to **“decrease the incidence of CIM in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC.”**
- Most common treatment-related toxicities listed on FDA label:
 - Fatigue
 - Hypocalcemia/hypokalemia/hypophosphatemia
 - Aspartate aminotransferase increased
 - Headache
 - Pneumonia

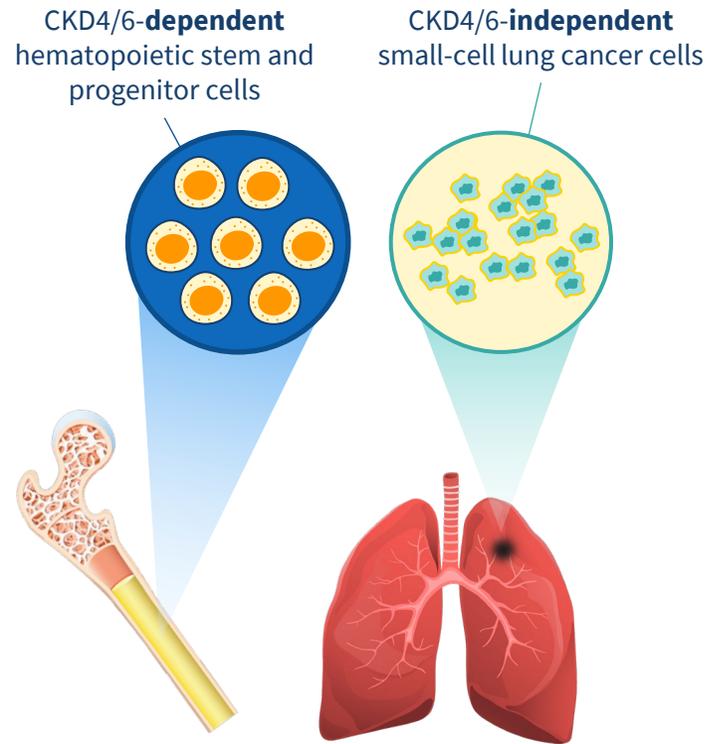
FDA Prescribing Information.



Trilaciclib Mechanism of Myeloprotection

Administer trilaciclib within 4 hours prior to the start of chemotherapy.

Platinum/etoposide- or topotecan-containing chemotherapy regimen



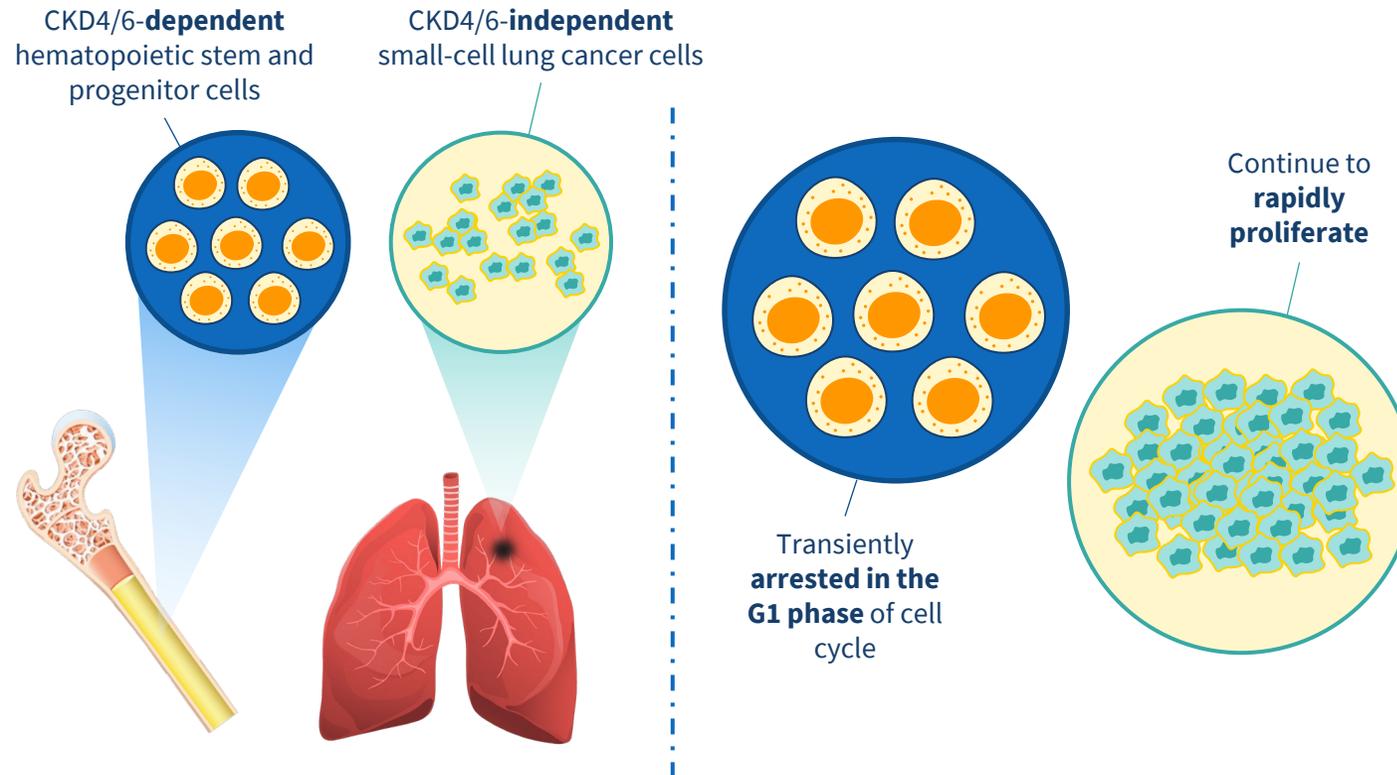
Weiss J, et al. *Clin Lung Cancer*. 2021.



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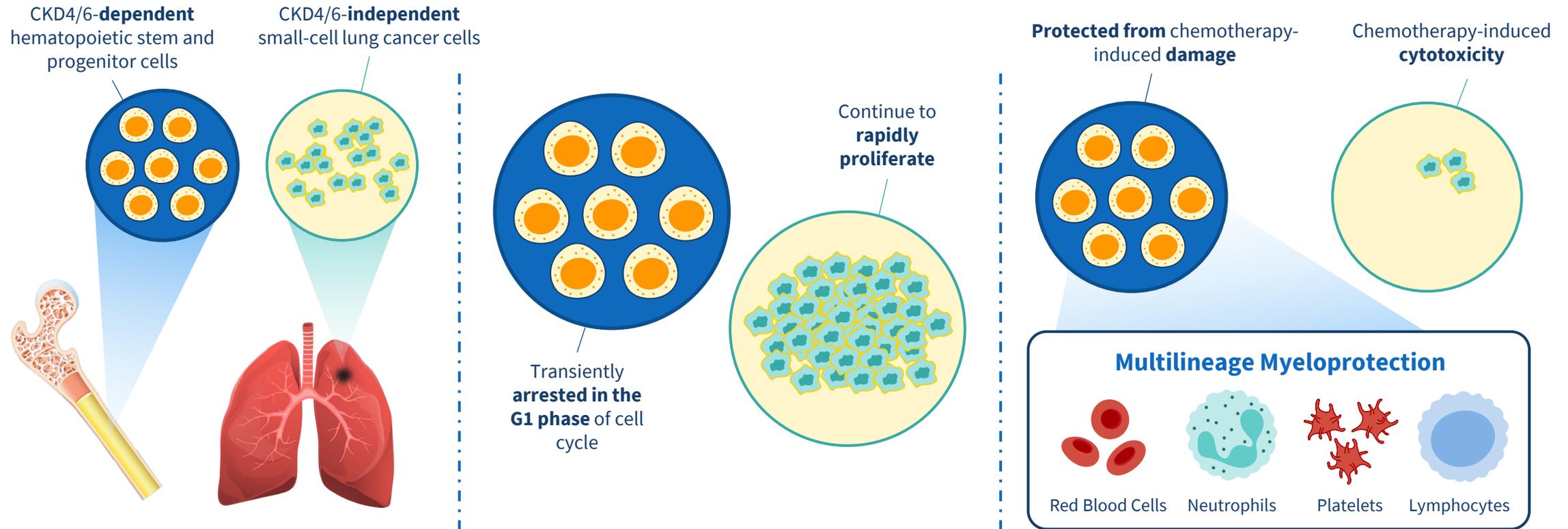
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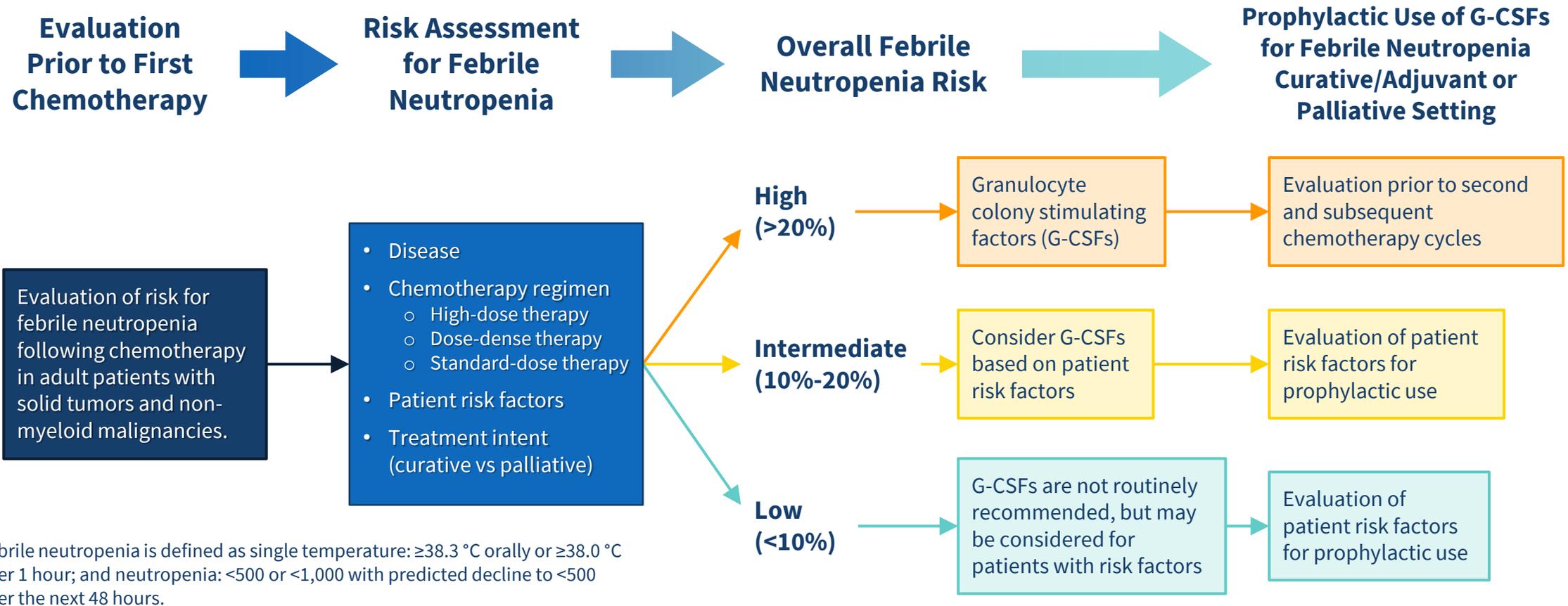
Platinum/etoposide- or topotecan-containing chemotherapy regimen



Weiss J, et al. *Clin Lung Cancer*. 2021.



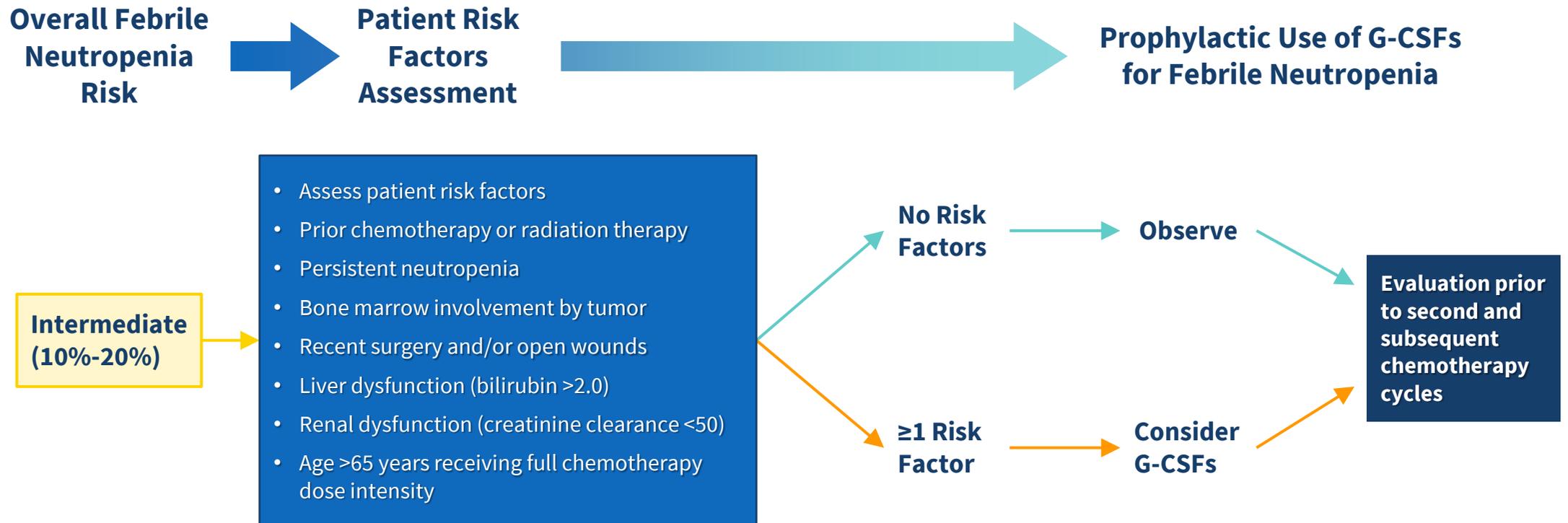
NCCN Guideline Recommendations



NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025.



NCCN Guideline Recommendations



NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025.



NCCN Guideline Recommendations

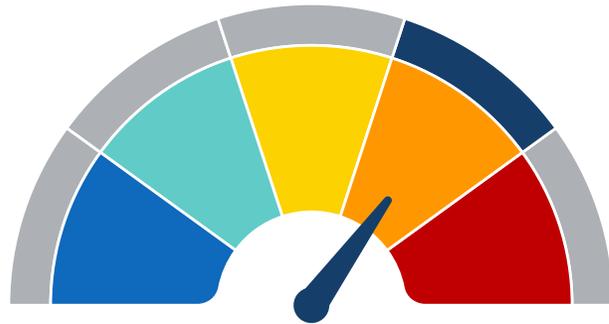
Trilaciclib

When platinum/etoposide +/- immune checkpoint inhibitor or a topotecan-containing regimen is used for ES-SCLC, trilaciclib is recommended as:

- **Prophylactic option to prevent CIM (category 2A)**
- **Prophylactic option to decrease the incidence of anemia (category 2B)**
- **Prophylactic option to reduce the need for RBC transfusions (category 2B)**

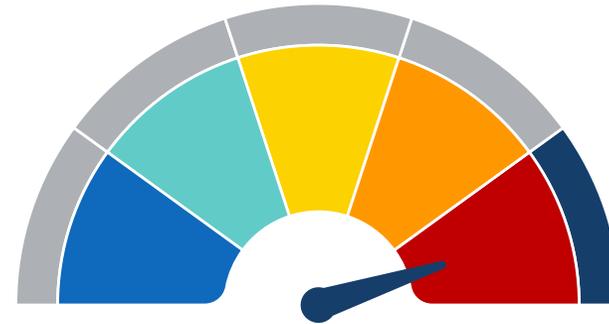


Risk for Febrile Neutropenia



Moderate Risk for Febrile Neutropenia

Carboplatin/Etoposide (SCLC)
Cisplatin/Etoposide (NSCLC)



High Risk for Febrile Neutropenia

Topotecan-Based Regimens

NCCN Clinical Practice Guidelines: Hematopoietic Growth Factors. Version 1.2025; NCCN Clinical Practice Guidelines: Small Cell Lung Cancer. Version 2.2026.



How Do the *NCCN* SCLC Guidelines View Chemotherapy-Induced Myelosuppression Prophylaxis?

“GM-CSF or G-CSF are not recommended during concurrent systemic therapy + RT.”

“Trilaciclib or G-CSF may be used as prophylactic options to decrease the incidence of chemotherapy-induced myelosuppression when administering platinum/etoposide ± immune checkpoint inhibitor-containing regimens or a topotecan-containing regimen for ES-SCLC.”



How Do the *ASCO* SCLC Guidelines View Chemotherapy-Induced Myelosuppression Prophylaxis?



“May use **trilaciclib or **G-CSF** if clinically indicated.”**

Kalemkerian G, et al. *J Clin Oncol*. 2025.



Achieving Myeloprotection in Real-World ES-SCLC Practice

An Illustrative Patient Case



Meet JR

- 54-yo male
- Recently diagnosed with ES-SCLC
- He is preparing to start 1L treatment (first appt scheduled for next week)
 - Carboplatin/etoposide/atezolizumab
 - Carboplatin AUC 5 day 1
 - Etoposide 100 mg/m² on days 1, 2, and 3
 - Atezolizumab 1,200 mg on day 1
 - 21-day cycles x 4
 - Followed by maintenance atezolizumab 1,200 mg
- **What do you tell JR about his risk for CIM?**
- **What do you recommend to help mitigate that risk and improve the quality of his care?**





Summary and Key Takeaways

- Cytopenias are a treatment limiting toxicity in small cell lung cancer.
- Growth factors (G-CSF) can effectively address neutropenia and neutropenia-related infections.
- Anemia and thrombocytopenia have remained with large unmet need (Transfusions, unclear role of growth factors).
- CDK4/6 Inhibition has been shown to be myeloprotective, reducing cytopenias and dependent complications across all 3 lines.
- Novel mechanisms include lymphocyte protection important for PD-L1 and DLL3 bispecific targeting



Post-Test



Claim Your CE Credit!

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using this QR code (or by visiting
<https://form.jotform.com/AcademyCME/25C26GRpost>)

Thank You!

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