Proactive Management of Myelosuppression in ES-SCLC

Evaluating Prophylactic CDK4/6 Inhibitor Therapy

Limitations of Traditional Reactive Treatment Strategies for Chemotherapy-induced Myelosuppression

Risk/adverse effects		Limitations
ESA RBC transfusion	Thromboembolic events Risk of infection, transfusion reactions, alloimmunization	Addresses only 1 cell lineage Initated after cytopenias develop (does not protect HSPCs) Does not prevent recurrent cytopenias Dose delays and/or reduction may still be needed
G-CSF	Bone pain	
Platelet transfusion	Transfusion reactions	Transient effects for RBC and platelet transfusion G-CSF cannot be given concurrently with chemotherapy

Proactive Prophylactic Approaches for Chemotherapy-induced Myelosuppression

Trilaciclib

Preserves multiple hematopoietic lineages by acting directly on HSCPs

G-CSF

Stimulates neutrophil precursors to reduce the risk of febrile neutropenia but does not:

- Target HSCPs
- Address other cell lineages

Mechanism of Action of CDK4/6 Inhibition

CDK4/6 inhibition induces transient G1 cell cycle arrest of HSPCs

- HSPCs: CDK4/6 dependent, preventing them from entering S-phase where they are vulnerable to cytotoxic damage
- SCLC cells: CDK4/6 independent and are not vulnerable to agents such as trilaciclib

Timing and Administration of Trilaciclib

Trilaciclib Administration

- **30 minute** IV infusion
- **Within 4 hours** of chemotherapy

Subsequent Treatment Days

<28 hours between interval doses of trilaciclib on sequential days

Skipped/Missed Chemotherapy

Skip and resume trilaciclib on next scheduled day of chemotherapy

Trilaciclib Discontinuation

Wait 96 hours from last dose of trilaciclib before resumption of chemotherapy

Efficacy of Trilaciclib in ES-SCLC

Levels of Evidence

Demonstrated Efficacy

Across multiple levels of evidence, trilaciclib vs placebo has demonstrated significant or positive trends in:

- Cytopenias across all cell lineages, including
  - Severe neutropenia (grade 4)
  - Duration of severe neutropenia, during cycle 1
  - Febrile neutropenia
  - Grade 3/4 neutropenia and thrombocytopenia
- Supportive care utilization across all cell lineages, including
  - G-CSF and ESA administration
  - RBC and platelet transfusions
- Chemotherapy cycle delays and dose reductions

Trilaciclib did not demonstrate detrimental effects on overall and progression-free survival

Trilaciclib was associated with a reduced need for hospitalizations due to myelosuppression or sepsis

Safety Data and Considerations for Trilaciclib

Most Common AEs in ≥5% Patients with ≥2% Higher Incidence Compared to Placebo

Symptoms	Trilaciclib (N=122)		Placebo (N=118)	
	Any grade, %	Grade ≥3, %	Any grade, %	Grade ≥3, %
Fatigue	34	3	27	2
Headache	13	0	9	0
Pneumonia	10	7	8	7
Rash	9	<1	6	0
Infusion-related reaction	8	0	2	0
Peripheral edema	7	0	4	<1
Upper abdominal pain	7	0	3	0
Thrombosis	7	3	2	2

Lab Abnormalities	Trilaciclib (N=122)		Placebo (N=118)	
	Any grade, %	Grade ≥3, %	Any grade, %	Grade ≥3, %
Hypocalcemia	24	<1	21	<1
Hypokalemia	22	6	18	3
Hypophosphatemia	21	7	16	2
Increased AST	17	<1	14	<1
Hyperglycemia	6	2	3	0

Drug-drug interactions

Trilaciclib is an OCT2, MATE1, and MATE-2K inhibitor

Cisplatin
Closely monitor for nephrotoxicity

Dalfampridine
Increased risk of seizures

Dofetilide
Increased risk of QT prolongation

Dose modifications

Hepatic impairment (moderate or severe)
Dose reduction

ILD/pneumonitis
Hold for grade 2 and permanently discontinue for grades ≥3

Injection-site reactions
Interrupt/slow/stop infusion or permanently discontinue based on AE severity

Acute hypersensitivity reaction
Stop and hold for grades 2 and permanently discontinue for grades ≥3

ABBREVIATIONS

AE: adverse event
AST: aspartate aminotransferase
CDK: cyclin-dependent kinase
ESA: erythropoiesis-stimulating agents
ES-SCLC: extensive-stage small cell lung cancer
G-CSF: granulocyte colony-stimulating factor
ILD: interstitial lung disease
MATE1: multidrug and toxin extrusion protein 1
MATE-2K: multidrug and toxin extrusion protein 2K
RBC: red blood cell
OCT2: organic cation transporter 2
SCLC: small cell lung cancer

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