



Administration of Trilaciclib

ICD-10 Coordination & Maintenance Committee Meeting

March 9, 2021



**Our solution:
Trilaciclib**

First-in-class
myelopreservation therapy
that has the potential to make
chemotherapy safer, improve
the patient experience, and in
some settings, help patients
live longer

Overview

- G1 Therapeutics' mission is to discover, develop and deliver innovative therapies that improve the lives of those affected by cancer.
- Specifically, G1 Therapeutics is studying the effects of its lead compound Trilaciclib, which can become a first-in-class therapy that improves clinical outcomes for people with cancer who are treated with chemotherapy.
 - Trilaciclib is a myelopreservation therapy that has the potential to mitigate chemotherapy induced myelosuppression (CIM) in Small Cell Lung Cancer (SCLC) patients receiving regimens containing platinum + etoposide +/- checkpoint inhibitor; or a topotecan-containing regimen.
 - In 2019, trilaciclib was granted Breakthrough Therapy Designation for the mitigation of clinically significant chemotherapy-induced myelosuppression in adult patients with SCLC.
 - In June 2020, G1 submitted an NDA. The NDA has been accepted for Priority Review by the FDA and assigned a PDUFA, or target action date, of February 15, 2021.

Trilaciclib: Description

- Trilaciclib works by arresting the hematopoietic stem and progenitor (HSPCs) bone marrow cells in the G1 phase of the cell cycle during chemotherapy exposure thereby protecting them for chemotherapy-induced damage.
- Further, trilaciclib is a selective, transient inhibitor of cyclin dependent kinases 4 and 6 (CDK4/6) with potential antineoplastic and chemoprotective activities.
- In preclinical models, CDK4/6 inhibition by trilaciclib also alters the tumor immune microenvironment through transient inhibition of lymphocytes that also rely on CDK4/6 activity (dependent) for proliferation.
 - The transient arrest of HSPCs and lymphocytes by trilaciclib during the administration of chemotherapy is thought to have a number of beneficial effects, including a reduction in chemotherapy-induced myelosuppression and preservation of immune function, as well as an enhanced immune response.
- There is only the generic name: Trilaciclib, which is a stand-alone procedure that is administered either intravenously or via a central line infusion.

Trilaciclib: Utilization

- Trilaciclib is for patients suffering from extensive stage small cell lung cancer (ES-SCLC) treated with platinum / etoposide-containing or topotecan-containing chemotherapy regimens.
- Trilaciclib is given via IV administration 30 minutes before chemotherapy on the days chemotherapy is given to reduce the treatment associated side effects which include neutropenia, anemia, thrombocytopenia, and the need for supportive care interventions and hospitalizations.
- Trilaciclib should be administered at a dose of 240 mg/m² as a 30-minute IV infusion no more than 4 hours prior to chemotherapy on each day chemotherapy is administered.
- Patients treated with trilaciclib are generally treated with 4 cycles of 21 days each, where days 1-3 of the cycle involve chemotherapy with a dose of trilaciclib administered in conjunction with the chemotherapy.
 - This is followed by an 18-day treatment holiday.
- Dosing is based on body surface area, 240 mg/m², with an average of 2 vials per patient. Vials are 300mg and typically 2 vials.

Trilaciclib: Site of Care

- Trilaciclib will be used in both the inpatient and outpatient sites of care.
 - Inpatient hospitalization is only expected to span one cycle.
 - Complications from chemotherapy-induced myelosuppression and its negative sequelae have been a long-standing challenge to management of patients with SCLC.
 - Current supportive care therapies are lineage-specific and administered after chemotherapy-induced damage has occurred.
- Based on the description and severity of these clinical conditions, the patient can be admitted.
 - Documentation for the administration of trilaciclib can be found in progress notes of the medical record and generally translates to the assignment of ICD-10-CM codes describing malignant neoplasm of bronchus and lung (C34.00 – C34.92)
- Trilaciclib is then administered proactively to preserve hematopoietic stem and progenitor cells during chemotherapy, thus improving its safety and tolerability of chemotherapy and the quality of life of patients receiving chemotherapy.
 - This administration is based on the results of three randomized, double-blind, placebo-controlled clinical studies demonstrating multilineage myelopreservation of patients with SCLC undergoing frontline or subsequent systemic therapy.
 - Administration of trilaciclib by intravenous infusion before each dose of chemotherapy was associated with significantly lower duration of severe neutropenia, occurrence of severe neutropenia, occurrence of febrile neutropenia, rescue with growth factors or blood transfusions (i.e., G-CSF, ESA, or red blood cell transfusions), and grade 3/4 decreased hemoglobin across three randomized, double-blind, placebo-controlled clinical trials of adult patients with SCLC.

Adverse Events-Trilaciclib

	Chemotherapy + Trilaciclib (N = 122)	Chemotherapy + Placebo (N = 118)	Relative Reduction in Event Rate (Trilaciclib vs. Placebo)
Event	Grades 3-4	Grades 3-4	Grades 3-4
Hematologic Adverse Reactions, N (%)			
Neutropenia	39 (32)	81 (69)	-54%
Febrile neutropenia	4 (3)	11 (9)	-67%
Anemia	20 (16)	40 (34)	-53%
Thrombocytopenia	22 (18)	39 (33)	-45%
Leukopenia	5 (4)	20 (17)	-76%
Other Events, N (%)			
Adverse events of special interest	2 (2)	2 (2)	-3%
Discontinuation Rate, N (%)			
Discontinuation due to TEAEs	11 (9)	13 (11)	-18%

Adverse events of special interests were most commonly grade 1 or 2 injection site reactions and phlebitis/thrombophlebitis. Trilaciclib is not a vesicant

The most common ARs (≥10%) of any grade in patients receiving trilaciclib occurring at the same or higher incidence than in patients receiving placebo by descending frequency were nausea, fatigue, dyspnea, pyrexia, headache, and decreased appetite.

Warnings and precautions may include: Injection-Site Reactions, Including Phlebitis and Thrombophlebitis, Acute Drug Hypersensitivity Reactions, Interstitial Lung Disease/Pneumonitis, & Embryo-Fetal Toxicity.