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Positive Quality Intervention: Trilaciclib (Cosela®) Management

Description: The purpose of this PQI is to describe the indication, pharmacology and dosing of trilaciclib.

Background: Trilaciclib is a CDK 4/6 inhibitor indicated to decrease the incidence of chemotherapy-induced myelosuppression in patients undergoing chemotherapy with a platinum/etoposide or topotecan containing regimen for extensive stage small cell lung cancer (ES-SCLC). It is administered prior to chemotherapy on all days of treatment. Trilaciclib is a transient inhibitor of CDK 4/6. Hematopoietic stem and progenitor cell (HSPC) proliferation is dependent on CDK 4/6 activity. In clinical studies, trilaciclib increased the percentage of cells arrested in the G1 phase of cell division for up to 32 hours post-infusion for all bone marrow progenitor subsets evaluated. This transient G1 arrest of HSPCs contributes to the myeloprotective effect of trilaciclib.[1] In the pivotal study (GIT28-05), treatment with trilaciclib decreased the incidence of severe neutropenia vs. placebo (2% vs 49%, P<0.0001). Mean duration of severe neutropenia in cycle 1 was also decreased (1 day vs 4.7 days, P<0.0001).[1] Additional clinical trials also showed benefits in decreased incidence of severe neutropenia vs. placebo. Secondary endpoints for the studies included red blood cell transfusions after week 5 and GCS-F support; although not statistically significant, trilaciclib decreased the need for platelet transfusions versus placebo. Clinically significant differences in the need for supplemental GCS-F support was seen in the trilaciclib treatment group versus placebo (0.149 events/cycle vs 0.280 events/cycle, respectively, P = 0.0145).[2]

PQI Process:[1]

- Identify patients who are at high risk for myelosuppression who will be receiving treatment for ES-SCLC with a platinum/etoposide or topotecan based regimen and recommend the use of trilaciclib
- Upon order of trilaciclib administration confirm appropriateness of therapy
- Review medication list for significant interactions (cisplatin, dofetilide and dalfampridine)
    - Trilaciclib is an inhibitor of organic cation transport (OCT2), multidrug and toxin extrusion1 (MATE1) and MATE-2K as coadministration these substrates may increase concentration of those drugs leading to increased serious or life-threatening toxicities
- Review the adverse events and recommended actions (see Supplemental Information)
- Infusion-site reactions including phlebitis and thrombophlebitis are possible and occurred in 56% of patients in clinical trials; monitor for signs and symptoms of injection-site reactions during the infusion
    - For mild to moderate injection-site reactions, flush line with at least 20 mL NS or D5W
    - For patient symptoms or discomfort, ice/cold packs or warm compresses can be used
- The most common adverse reactions are fatigue, hypocalcemia, hypokalemia, hypophosphatemia, increased aspartate aminotransferase, headache, and pneumonia
- If trilaciclib is discontinued, wait 96 hours from the last dose of trilaciclib before resuming treatment
- Dosing:
    - Trilaciclib 240 mg/m^2 is given over 30 minutes within 4 hours prior to start of chemotherapy
        - The interval between doses on sequential days should not be more than 28 hours
    - Reconstitute 300 mg vial with 19.5 mL NS or D5W for a concentration of 15 mg/mL
        - The diluted trilaciclib solution will be clear yellow
    - Further diluted with NS or D5W for a final concentration between 0.5-3 mg/mL with in-line 0.2-micron filter (do not use polytetrafluoroethylene inline filter)

Patient-Centered Activities:

- Provide written and verbal patient education regarding trilaciclib
- Instruct the patient to notify the nurse of any irritation, swelling, pain, redness, tenderness, itchy skin that feels warm to the touch around the injection site during the infusion[2]
- Educate patients to report worsening respiratory issues as interstitial lung disease/pneumonitis is a potential adverse effect that would warrant quick identification and treatment
- Females of childbearing age should be informed that trilaciclib can harm an unborn baby
    - Effective method of birth control is necessary during treatment and ≥ 3 weeks after the last dose
- Counsel patient on disease state, treatment regimen, adverse reactions, and verify understanding

Supplemental Information

Adverse Reaction	Severity	Recommended Action
Injection-site reactions, including phlebitis and thrombophlebitis	Grade 3: Ulceration or necrosis; severe tissue damage; operative intervention indicated OR Grade 4: Grade 4: Life-threatening consequences; urgent interventions indicated	Stop infusion and permanently discontinue
Acute drug hypersensitivity	Grade 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living (ADL)	Stop infusion and hold trilaciclib until recovery to ≤ Grade 1 or baseline; then consider resuming trilaciclib If Grade 2 recurs, permanently discontinue
	Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL OR Grade 4: Life-threatening consequences; urgent intervention indicated	Permanently discontinue
ILD/Pneumonitis	Grade 2 - Symptomatic	Hold trilaciclib until recovery to ≤ Grade 1 or baseline; consider resuming trilaciclib If Grade 2 recurs, permanently discontinue
	Grade 3: Severe symptoms; limiting self-care ADL; oxygen indicated OR Grade 4: Life-threatening respiratory compromise; urgent intervention indicated	Permanently discontinue
Other toxicities	Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL	Hold trilaciclib until recovery to ≤ Grade 1 or baseline; consider resuming trilaciclib If Grade 3 recurs, permanently discontinue
	Grade 4: Life-threatening consequences; urgent intervention indicated	Permanently discontinue

IV Infusion Bag Material	Diluent	Diluted Storage Duration
Polyvinyl chloride (PVC), Ethylene vinyl acetate (EVA), Polyolefin (PO), or Polyolefin/polyamide (PO/PA)	D5W	Up to 12 hours at 20°C to 25°C (68°F to 77°F)
PVC, EVA, or PO	NS	Up to 8 hours at 20°C to 25°C (68°F to 77°F)
PO/PA	NS	Up to 4 hours at 20°C to 25°C (68°F to 77°F)

References:

1. Cosela® (trilaciclib) Package Insert.
2. Cosela® (trilaciclib) for chemotherapy induced myelosuppression in Adult patients with Extensive-Stage Small cell lung cancer. AMCP DOSSIER 2/18/2021.