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. 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). Additional clinical trials also showed benefits in decreased incidence of severe neutropenia vs. placebo. Secondary endpoints for the studies included red blood cell (RBC) 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).

PQI Process:
- 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 with that chemotherapy regimen
- Upon order of trilaciclib administration confirm appropriateness of therapy
- Review patient medication list as significant interactions are possible with cisplatin, dofetilide and dalfampridine. Trilaciclib is an inhibitor of organic cation transport (OCT2), multidrug and toxin extrusion1 (MATE1) and MATE-2K. Coadministration with OCT2, MATE1 and MATE-2K substrates may increase concentration and levels 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 the trilaciclib treated 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 depending institutional policy/preferences
- The most common adverse reactions are fatigue, hypocalcemia, hypokalemia, hypophosphatemia, aspartate aminotransferase increased, headache, and pneumonia
- If trilaciclib is discontinued, wait 96 hours from the last dose of trilaciclib before resumption of chemotherapy only

Important notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.
PQI Process Continued:

- **Dosing:**
  - Trilaciclib 240 mg/m² is given over 30 minutes within 4 hours prior to start of chemotherapy on each day that it is given
    - The interval between trilaciclib doses on sequential days should not be more than 28 hours
  - Trilaciclib is supplied as a 300 mg vial and must be reconstituted with 19.5 mL NS or D5W for a concentration of 15 mg/mL
  - The diluted trilaciclib solution will be clear yellow
  - Trilaciclib must be further diluted in either NS or D5W for a final concentration between 0.5-3 mg/mL² with in-line 0.2 micron filter (do not use polytetrafluoroethylene inline filter)

Patient Centered Activities:

- Provide 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 infusion²
- 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 for at least 3 weeks after the last dose
- Counsel patient on disease state, treatment regimen, adverse reactions, and verify understanding
- Provide patient with treatment calendar outlining planned treatment schedule

Supplemental Information

Table 1

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Severity</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection-site reactions, including phlebitis and thrombophlebitis</td>
<td>Grade 3: Ulceration or necrosis; severe tissue damage; operative intervention indicated OR Grade 4: Grade 4: Life-threatening consequences; urgent interventions indicated</td>
<td>Stop infusion and permanently discontinue trilaciclib</td>
</tr>
<tr>
<td>Acute drug hypersensitivity</td>
<td>Grade 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living (ADL)</td>
<td>Stop infusion and hold trilaciclib until recovery to ≤Grade 1 or baseline; then consider resuming trilaciclib • If Grade 2 recurs, permanently discontinue trilaciclib</td>
</tr>
<tr>
<td></td>
<td>Grade 3: Severe or medically significant but not immediately life-threatening;</td>
<td>Permanently discontinue trilaciclib</td>
</tr>
</tbody>
</table>

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hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL 
OR 
Grade 4: Life-threatening consequences; urgent intervention indicated

ILD/Pneumonitis

<table>
<thead>
<tr>
<th>Grade 2 - Symptomatic</th>
<th>Hold trilaciclib until recovery to ≤Grade 1 or baseline; consider resuming trilaciclib</th>
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</thead>
<tbody>
<tr>
<td>Grade 3: Severe symptoms; limiting self-care ADL; oxygen indicated OR Grade 4: Life-threatening respiratory compromise; urgent intervention indicated (ex. tracheotomy or intubation)</td>
<td>Permanently discontinue trilaciclib</td>
</tr>
</tbody>
</table>

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 trilaciclib |
| Grade 4: Life-threatening consequences; urgent intervention indicated | Permanently discontinue trilaciclib |

![Table 2](image)

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

References:
3. Cosela™ (trilaciclib) for chemotherapy induced myelosuppression in Adult patients with Extensive-Stage Small cell lung cancer. AMCP DOSSIER 2/18/2021.