Positive Quality Intervention: Loncastuximab tesirine-lpyl (Zynlonta®) in Relapsed/Refractory Large B-Cell Lymphoma

Description: The purpose of this PQI is to discuss the clinical considerations around the use of loncastuximab tesirine-lpyl (Zynlonta®) to optimize the outcomes for patients with relapsed/refractory large B-cell lymphoma.

Background: Loncastuximab tesirine-lpyl is a CD19 directed antibody-drug conjugate with a pyrrolobenzodiazepine (PBD) dimer payload. The PBD dimer acts as an alkylating agent and has a relatively short half-life, decreasing likelihood of accumulation and reducing overall systemic toxicity. On April 23, 2021, loncastuximab tesirine-lpyl received FDA-approval for the management of relapsed/refractory large B-cell lymphoma (including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, or high-grade B-cell lymphoma) following 2 or more lines of prior systemic therapy. Approval was based on data from the phase 2, multicenter, single-arm LOTIS-2 study demonstrating an overall response rate of 48.3% in 145 treated patients, half of whom had a complete response.

Other key findings:
- Median time to response = 41 days; median duration of response = 10.3 months
- Median treatment cycles = 3 (range 1 – 15)
- Overall acceptable safety profile with a few notable considerations:
  - Hematologic toxicities: neutropenia (26%), thrombocytopenia (18%)
  - Effusions and edema related to the PBD dimer did occur in 31% of patients, but were generally low grade; see below for considerations around preventative corticosteroid use
  - Grade ≥3 elevations of gamma-glutamyltransferase (17%)
  - Infusion-related reactions were uncommon (5%)
- No signal indicating CD19-loss after loncastuximab tesirine-lpyl was found in a small cohort of progressing patients who were able to proceed to CAR T-cell therapy

PQI Process: Use of loncastuximab tesirine-lpyl should include the following safety considerations
- Verification of dosage, schedule, and concomitant conditions
  - Recommended dosage is 0.15 mg/kg IV over 30 minutes on Day 1 of cycles 1 and 2, then 0.075 mg/kg IV over 30 minutes on Day 1 of cycles 3 and onward; cycle length is 21 days
    - Use total body weight to determine dose, unless BMI ≥ 35 kg/m² or use adjusted body weight 35 kg/m² times (height in meters
  - Pregnancy testing is recommended in women of childbearing potential
- Ensure appropriate supportive care accompanies orders for loncastuximab tesirine-lpyl
  - Dexamethasone 4 mg by mouth orally or intravenously twice daily x 3 days (day prior to infusion, day of infusion, and day after infusion) to reduce the risk of edema and effusions
    - If patient forgets to take doses the day prior to loncastuximab tesirine-lpyl, then dexamethasone dose should be given at least 2 hours prior to infusion
- Preparation and administration
  - Add loncastuximab tesirine-lpyl in a 50 mL infusion bag containing 5% Dextrose Injection, USP
    - Diluted product may be stored in the refrigerator (2°C to 8°C) for up to 24 hours or room temperature (20°C to 25°C) for up to 8 hours
  - Administer as a 30-minute intravenous infusion through a dedicated infusion line using a sterile, non-pyrogenic, low-protein binding in-line filter (0.2 – 0.22 micron pore size)
• Review patient’s medications for drug-drug interactions
  o The PBD dimer component is a substrate of P-glycoprotein (P-gp)

### Adverse Events and Management

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Severity</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td><strong>Hematologic Toxicities</strong></td>
<td></td>
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<tr>
<td>Neutropenia</td>
<td>≥ Grade 3</td>
<td>Withhold loncastuximab tesirine-lpy until ANC ≥ 1000</td>
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<td></td>
<td></td>
<td>Use of granulocyte colony stimulating factors as management and/or as prevention</td>
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<tr>
<td></td>
<td>Absolute Neutrophil Count (ANC) &lt; 1000</td>
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<tr>
<td>Thrombocytopenia</td>
<td>≥ Grade 3</td>
<td>Withhold loncastuximab tesirine-lpy until Platelet Count ≥ 50,000</td>
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<tr>
<td></td>
<td>Platelet Count &lt; 50,000</td>
<td></td>
</tr>
<tr>
<td><strong>Non-Hematologic Toxicities</strong></td>
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<td></td>
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<tr>
<td>Edema/Effusion</td>
<td>≥ Grade 2</td>
<td>Withhold loncastuximab tesirine-lpy until toxicity resolves to ≤ Grade 1</td>
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<td>Use of spironolactone with or without a loop diuretic can be considered for edema management</td>
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<td>Consider diagnostic imaging and medical management with symptoms of pleural effusion or pericardial effusion and/or ascites</td>
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<tr>
<td>Cutaneous Reactions/Rash</td>
<td>≥ Grade 3</td>
<td>Withhold loncastuximab tesirine-lpy until resolved</td>
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<tr>
<td></td>
<td></td>
<td>Consider dermatology consult</td>
</tr>
<tr>
<td>Infection</td>
<td>≥ Grade 3</td>
<td>Withhold loncastuximab tesirine-lpy until resolved</td>
</tr>
<tr>
<td>Other Adverse Reactions</td>
<td>≥ Grade 3</td>
<td>Withhold loncastuximab tesirine-lpy until toxicity resolves to ≤ Grade 1</td>
</tr>
</tbody>
</table>

### Dose Modifications

• Reduce dose by 50% if treatment is delayed 3 weeks or longer due to treatment-related toxicity
  o If toxicity requiring dose reduction occurs following second dose of 0.15 mg/kg (Cycle 2), proceed with planned dose of 0.075 mg/kg with Cycle 3

### Patient-Centered Activities:

• Provide [Intravenous Cancer Treatment Education (IVE) Sheet](#)
  o Consider providing treatment calendar and include dosing for dexamethasone for the day before, day of, and day after each infusion
  o Educate patients on the signs of fluid overload (edema and effusions) and to contact their healthcare provider for swelling, weight gain, and shortness of breath or labored breathing
  o Encourage patient to report and signs or symptoms of infection including fever, chills, and upper respiratory symptoms such as cough or difficulty breathing
  o Advise patient to minimize sun exposure, wear sun-protective clothing, and to use sunscreen as sunlight can make rash/itching worse
  o Inform patients of reproductive risks and importance of appropriate contraception to avoid becoming pregnant or fathering a child while receiving loncastuximab tesirine-lpy

• Patient Assistance: [NCODA Financial Assistance Tool](#)

### References:

1. Zynlonta (loncastuximab tesirine-lpy) [package insert].