Positive Quality Intervention: Isatuximab-irfc (Sarclisa®) In Patients with Relapsed/Refractory Multiple Myeloma

Description: The purpose of this PQI is to discuss the option of using isatuximab-irfc with pomalidomide and dexamethasone in patients with relapsed/refractor multiple myeloma (RRMM) who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor or in combination with carfilzomib and dexamethasone in patients with RRMM who have received 1 to 3 prior lines of therapy.

Background: Isatuximab-irfc is an intravenous infused monoclonal antibody which selectively binds to the CD38 glycoprotein found on the surface of malignant plasma cells. Isatuximab-irfc has multiple mechanisms of action. ICARIA-MM was a phase 3 trial which compared the regimen of isatuximab-irfc plus pomalidomide and low dose dexamethasone to pomalidomide plus low dose dexamethasone alone in patients who received two or more prior therapies including lenalidomide and a proteasome inhibitor. The triplet therapy of isatuximab-irfc plus pomalidomide and low dose dexamethasone reduced the risk of disease progression or death by 40% compared to pomalidomide plus dexamethasone alone. In the IKEMA study, isatuximab-irfc plus carfilzomib and dexamethasone was compared to carfilzomib and dexamethasone alone. This combination reduced the risk of disease progression or death by 45% compared to carfilzomib and dexamethasone alone.

PQI Process:
- Pre-medication is recommended to reduce risk of infusion related reactions
  - Dexamethasone 40 mg either oral or IV x 1 dose; if patient is ≥ 75 years then give 20 mg
  - Acetaminophen 650 mg-1000 mg x 1 dose
  - H2 antagonist x 1 dose (e.g. famotidine 20 mg)
  - Diphenhydramine 25 mg-50 mg orally or IV (IV route is preferred for the first four infusions)
  - Review institutional policy to consider using montelukast (usage not required)
- Verify dosing of isatuximab-irfc is 10 mg/kg intravenous infusion every week for 4 weeks (induction) followed by every 2 weeks in combination with pomalidomide and dexamethasone or carfilzomib and dexamethasone until disease progression or unacceptable toxicity
  - Dosing is based on patient’s actual body weight at the beginning of each cycle
- Isatuximab-irfc is available in 100 mg/5mL vials and 500 mg/25 mL vials
- Preparation: isatuximab-irfc is compatible with 0.9% Sodium Chloride (NS) and 5% Dextrose (D5W)
- The infusion bag may be gently swirled to create a homogenous mixture *Do Not Shake*
- Binding of isatuximab-irfc to CD38 of red blood cells may result in a false positive indirect Coombs test; type and cross prior to first infusion

Table 1: Rate of infusion for isatuximab-irfc

<table>
<thead>
<tr>
<th></th>
<th>Volume</th>
<th>Initial rate</th>
<th>No infusion reaction</th>
<th>Rate Increment</th>
<th>Maximum Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>First infusion</td>
<td>250 mL</td>
<td>25 mL/hr</td>
<td>For 60 minutes</td>
<td>25 mL/hr every 30 minutes</td>
<td>150 mL/hr</td>
</tr>
<tr>
<td>Second Infusion</td>
<td>250 mL</td>
<td>50 mL/hr</td>
<td>For 30 minutes</td>
<td>50 mL/hr for 30 minutes then increase by 100 mL/hr every 30 minutes</td>
<td>200 mL/hr</td>
</tr>
<tr>
<td>Subsequent Infusions</td>
<td>250 mL</td>
<td>200 mL/hr</td>
<td>-</td>
<td>-</td>
<td>200 mL/hr</td>
</tr>
</tbody>
</table>

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Patient-Centered Activities:
- Patient Education
  - Infusion related reactions may occur (38-46%)\(^3,6\) with the administration of isatuximab-irfc. These usually occur with the first infusion and in most cases, resolve on the same day. Infusion reactions may include difficulty breathing, cough, chills and nausea and should counsel patient to report symptoms\(^4\)
  - Coordinate with patient and outside pharmacy (if needed) filling of oral medication(s)
  - Discuss diarrhea management
    - See Oncolytic Induced Diarrhea PQI and OCE Supplemental Sheet
- Monitoring
  - Monitor blood counts and blood pressure
  - Monitor for symptoms of low grade fever, chills, sweating, sore throat, cough/shortness of breath
- Patient Assistance: NCODA Financial Assistance Tool

References:
5. Sarclisa®(isatuximab-irfc) Package Insert.