Written By: Jon Suyko, PharmD, BCPS
UCHealth Highlands Ranch

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 proteosome 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.[3] 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.[4] 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.[6]

PQI Process:

- Pre-medication is recommended to reduce risk of infusion related reactions[5]
  - 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[5]

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

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:

1. Trudel, Suzanne. "Incorporating Isatuximab in the Treatment of Multiple Myeloma." The Lancet, vol. 394, 7 Dec. 2019, pp. 2045–2046.
2. Moreno, Laura, et al. "The Mechanism of Action of the Anti-CD38 Monoclonal Antibody Isatuximab in Multiple Myeloma." Clinical Cancer Research, vol. 25, no. 10, 15 May 2019.
3. Martin, Thomas, et al. "Therapeutic Opportunities with Pharmacological Inhibition of CD38 with Isatuximab." Cells, vol. 8, no. 1522, 26 Nov. 2019.
4. Attal, Prof. Michael, et al. "Isatuximab plus Pomalidomide and Low-Dose Dexamethasone versus Pomalidomide and Low-Dose Dexamethasone in Patients with Relapsed and Refractory Multiple Myeloma (ICARIA-MM): a Randomised, Multicentre, Open-Label, Phase 3 Study." The Lancet, vol. 394, no. 10214, 7 Dec. 2019, pp. 2096–2107.
5. Sarclisa®(isatuximab-irfc) Package Insert.
6. Moreau, P., Dimopoulos, M.-A., Mikhael, J., Yong, K., Capra, M., Facon, T., Hajek, R., Špička, I., Baker, R., Kim, K., Martinez, G., Min, C.-K., Pour, L., Leleu, X., Oriol, A., Koh, Y., Suzuki, K., Risse, M.-L., Asset, G., … Ozkalemkas, F. (2021, June 4). Isatuximab, carfilzomib, and dexamethasone in relapsed multiple myeloma (Ikema): A Multicentre, open-label, Randomised Phase 3 trial. The Lancet. Retrieved September 27, 2022, from https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00592-4/fulltext.