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Positive Quality Intervention: Tafasitamab-cxix (Monjuvi®) for Relapsed/Refractory Diffuse Large B-Cell Lymphoma

Description: The purpose of this PQI is to discuss the clinical considerations of tafasitamab-cxix (Monjuvi®) to optimize the outcomes for patients with relapsed/refractory (R/R) diffuse large B-Cell lymphoma (DLBCL).

Background: DLBCL is an aggressive lymphoma and is the most common subtype of non-Hodgkin's lymphoma (NHL) in the United States, accounting for approximately 22% of newly diagnosed B-Cell NHL cases each year.[1] The prognosis for patients with R/R disease remains poor, with expected survival of less than 8 months.[2] Tafasitamab-cxix is a CD19-directed cytolytic antibody as a preferred regimen indicated in combination with lenalidomide for the treatment of adult patients with R/R DLBCL who are not eligible for autologous stem cell transplant.[3,4] It was approved under the FDA accelerated approval pathway based on overall response rate and confirmatory trials are currently underway. Efficacy of this regimen was based on the L-MIND study which was a multicenter, open-label, single arm, phase 2 study enrolling adult patients with R/R DLBCL after 1-3 prior systemic therapies, one of which being an anti-CD20 therapy.[5] The primary endpoint of the study was objective response rate with key secondary endpoints being duration of response, progression-free survival, and overall survival. At a median follow-up of 13.2 months, 48 of the 80 enrolled patients (60%, 95% CI 48-71%) had an objective response with 34 patients (43%) achieving a complete response. An additional 11 patients (14%) had stable disease which equates to a disease control rate of 74%. The most common Grade ≥ 3 adverse events were neutropenia (48%), thrombocytopenia (17%), and febrile neutropenia (12%). A large phase 2/3 randomized trial, B-MIND, is underway to compare tafasitamab-cxix plus lenalidomide versus rituximab plus bendamustine in patients with R/R DLBCL.[6]

PQI Process: Upon the receipt of a new prescription of tafasitamab-cxix for R/R DLBCL:

- Verify pre-medications: acetaminophen, H1 receptor antagonist, H2 receptor antagonist, and a corticosteroid should be given 30-120 minutes prior to the first 3 infusions (if no reaction occurs during the first 3 infusions, then optional with subsequent infusions)
- Verify tafasitamab-cxix dosing:
  - Cycle 1: 12 mg/kg on days 1, 4, 8, 15, 22
  - Cycles 2-3: 12 mg/kg on days 1, 8, 15, 22
  - Cycle 4+: 12 mg/kg on days 1 and 15
- Verify lenalidomide dosing: 25 mg once daily on days 1-21 of a 28-day cycle for up to 12 cycles
  - Ensure all lenalidomide REMS requirements are met
  - Dose adjustments needed for baseline renal dysfunction
- Monitoring:
  - CBC and CMP: baseline and prior to each treatment cycle
  - Consider granulocyte colony-stimulating factor administration (intermediate risk)
- Preparation:
  - Tafasitamab-cxix is supplied as 200 mg vials
  - Reconstitute each 200 mg vial with 5 mL of sterile water (final concentration of 40 mg/mL)
  - Dilute to desired volume with 250 mL of 0.9% sodium chloride (final concentration of 2-8 mg/mL)
  - Store the diluted solution refrigerated for up to 18 hours followed by up to 12 hours at room temperature or at room temperature for up to 12 hours
  - Protect from light during storage

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- Administration:
  - First infusion: administer intravenously at 70 mL/h for the first 30 minutes then increase the rate so that the infusion is administered over 1.5-2.5 hours
  - Subsequent infusions: administer over 1.5-2 hours
  - Do not co-administer other medications through the same infusion line as tafasitamab-cxix
- Adverse Event Management: *see supplement section*

Patient Centered Activities:

- Provide written and verbal patient education
  - Review the most common adverse effects: neutropenia, fatigue, anemia, diarrhea, cough, thrombocytopenia, fever, peripheral edema, respiratory tract infection, and decreased appetite
  - Instruct patient to report any adverse events to the care team
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Lymphoma Research Foundation. Understanding diffuse large B-cell lymphoma. 2020; Available at: https://lymphoma.org/wp-Content/uploads/2018/05/LRF_FACTSHEET_DIFFUSE_LRG_BCELL_LYMPHOMA_DLBCL.pdf. Accessed May 27, 2021.
2. Crump M, Neelapu SS, Farooq U, et al. Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study. *Blood*. 2017;130(16):1800-1808.
3. Monjuvi (tafasitamab) [prescribing information].
4. NCCN Guidelines Diffuse Large B-Cell Lymphoma.
5. Salles G, Duell J, Gonzalez Barca E, et al. Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicentre, prospective, single-arm, phase 2 study. *Lancet Oncol*. 2020 Jul;21(7):978-988.
6. Nowakowski GS, Belada D, Molina L, et al. B-MIND: MOR208 plus bendamustine (BEN) versus rituximab (RTX) plus BEN in patients with relapsed or refractory (R-R) diffuse large B-cell lymphoma (DLBCL): an open-label, randomized phase II/III trial. *J Clin Oncol*. 2017;35(Supplement_15):TPS7571.

Supplemental Information:

Adverse Reaction Management

Adverse Reaction	Severity	Dosage Modification
Hematologic toxicity	Platelets ≤ 50,000/mm^3	Hold tafasitamab-cxix (and lenalidomide), monitor CBC weekly until platelet count is ≥50,000/mm^3, then resume tafasitamab-cxix at the same dose (and lenalidomide at a reduced dose).
	Neutrophil count ≤ 1,000/mcL for at least 7 days **or** neutrophil count ≤ 1,000/mcL with fever (temp ≥100.4°F or ≥38°C) **or** neutrophil count < 500/mcL	Hold tafasitiamab-cxix (and lenalidomide), monitor CBC weekly until neutrophil count is ≥1,000/mcl, then resume tafasitamab-cxix at the same dose (and lenalidomide at a reduced dose).
Infusion-related reaction	Grade 2 (moderate)	Interrupt infusion immediately and manage symptoms. Once resolved or reduced to Grade 1, resume infusion at 50% rate at which reaction occurred. If no further reaction within 1 hour and vital signs are stable, may increase infusion rate every 30 minutes as tolerated to rate at which the reaction occurred.
	Grade 3 (severe)	Interrupt infusion immediately and manage symptoms. Once resolved or reduced to Grade 1, resume infusion at 25% rate at which reaction occurred. If no further reaction within 1 hour and vital signs are stable, may increase infusion rate every 30 minutes as tolerated to a maximum of 50% rate at which the reaction occurred. Stop immediately if reaction returns upon rechallenge.
	Grade 4 (life threatening)	Stop infusion immediately and permanently discontinue.