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Positive Quality Intervention: Initiating Mosunetuzumab-axgb (Lunsumio™) in Relapsed/Refractory Follicular Lymphoma

Description: The purpose of this PQI is to provide background on bispecific T-cell engagement and discuss the proper patient selection and prevention of adverse events related to the administration of mosunetuzumab-axgb in patients with relapsed/refractory (R/R) follicular lymphoma (FL) after two or more lines of systemic therapy.

Background: Follicular lymphoma (FL) accounts for about 22% of newly diagnosed non-Hodgkin's lymphoma (NHL) and is the most common subtype of indolent NHL.[1] Despite its indolent nature and generally favorable response to frontline therapies, patients with FL who do not respond to upfront therapies and/or relapse after initial treatment tend to have unfavorable outcomes.[1,2] Mosunetuzumab-axgb is a bispecific CD20-directed CD3 T-cell engager indicated for the treatment of adult patients with R/R FL after two or more lines of systemic therapy. Its mechanism of action is unique from that of traditional chemotherapy in that it utilizes the patient's immune system by binding to CD3 receptors expressed on the surface of T-cells while also binding to CD20 expressed on the surface of lymphoma cells and some healthy B-lineage cells.[3] By binding to these receptors on a patient's own T-cells, the drug aids the immune system in recognizing the cancer cells due to simultaneous binding to CD20, thereby leading to B-cell (cancer cell) destruction through activation of immune response. Accelerated FDA approval of mosunetuzumab-axgb was based on an 80% overall response rate, including a 60% complete response rate, in patients with R/R FL after 2 or more prior therapies as demonstrated in the Phase II GO29781 trial.[4] Cytokine release syndrome (CRS) is a well-known adverse effect of bispecific T-cell engager therapy and was observed at a rate of 44% in the GO29781 trial, most of which were Grade 1 or 2 in severity (26% and 17%, respectively) and typically occurred within the first cycle of treatment.[4] Neurologic toxicity, another serious adverse effect associated with bispecific T-cell engager therapies, occurred in 39% of patients, with Grade 3 neurologic toxicity occurring in 3% of patients.[3,4] Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) is a serious subtype of neurologic toxicity and was reported in 1% of patients (Grade 1 and 2 only).[3,4] Neutropenia and infection risk is another adverse effect of interest that should be monitored and managed judiciously; Grade 3–4 neutropenia or neutrophil count decrease occurred in 27% of patients in clinical trial.[3,4] Hospitalization is not mandatory with administration. The safety profile of mosunetuzumab-axgb allows for initiation as an outpatient regimen. However, hospitalization is recommended for management of select adverse events.[3,4]

PQI Process: Upon receiving order for mosunetuzumab-axgb administration

- Confirm appropriateness utilizing the patient's chart – R/R FL after ≥2 lines of systemic therapy
- Ensure appropriate dose and schedule based on day of treatment, cycle, and any treatment delays (see Supplemental Information Table 1 and Table 2), which aims to reduce risk of CRS
    - Administer for a total of 8 cycles or 17 cycles depending on response, unless a patient experiences unacceptable toxicity or disease progression
    - CRS risk is highest during cycle 1, especially day 1 and day 15; however, CRS can occur at any point in therapy
- Ensure appropriate pre-medications are ordered for CRS and infusion reaction prevention
    - Corticosteroid 60 minutes pre-infusion and antihistamine and antipyretic 30 minutes pre-infusion
        - A**ll patients** in **Cycle 1 and Cycle 2**
        - Any patients who experienced **CRS with the prior dose**, regardless of cycle (e.g., Cycle 3 Day 1 if patient experienced CRS with Cycle 2 Day 1)
        - All patients repeating step-up dosing outside of Cycles 1 and 2
- Review adverse effects and necessary interventions as needed (see Product Labeling)

- Consider supportive care measures for patients at risk for tumor lysis syndrome (especially during Cycle 1 where the risk is highest) or infection
- Note risk of tumor flare, which can include pleural effusions and/or swelling at lymphoma sites

Patient-Centered Activities:

- Educate patient on schedule of administration: Highlight weekly step-up dosing with Cycle 1
- Discuss with patient the risk of Cytokine Release Syndrome and to report any symptoms that include, but are not limited to: fever, chills, fast or irregular heartbeat, tiredness or weakness, difficulty breathing, headache, confusion dizziness or light-headedness, nausea, and vomiting
- Discuss with patient the risk of neurotoxicity/ICANS and to report any symptoms that include, but are not limited to: headache, peripheral neuropathy, dizziness, and mental status changes (confusional state, disturbance in attention, cognitive disorder, delirium, somnolence)
- Educate the patient on risk of infection associated with bone marrow suppression and how to mitigate, including contacting care team for fever, as above with CRS
- Educate the patient on the signs of tumor flare, pleural effusions, and/or swelling at lymphoma sites
- Monitor lab values before each cycle and prior to each dose during step-up schedule, focusing on neutropenia, thrombocytopenia, electrolyte abnormalities (including phosphorus) and changes in liver function tests and/or blood glucose, at minimum
- Recommend female patient use effective contraception during therapy and for 3 months after last dose
- Patient Financial Assistance: NCODA Financial Assistance Tool

References:

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). B-Cell Lymphomas. Version 5.2023. Published July 7, 2023. Accessed August 24, 2023. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf.
2. Hill BT. Follicular lymphoma background and introduction to a patient case. OncLive. Published October 27, 2022. Accessed August 24, 2023. https://www.onclive.com/view/follicular-lymphoma-background-and-introduction-to-a-patient-case Onc Live.
3. Lunsumio ™ (mosunetuzumab-axgb) [Prescribing Information].
4. Budde LE, Sehn LH, Matasar M, et al. Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicentre, phase 2 study. *Lancet Oncol*. 2022 Agu;23(8):1055-1065.

Supplemental Information:

Table 1: Recommended mosunetuzumab-axgb Dose and Schedule (21-day Treatment Cycles)

Day of treatment		Dose of mosunetuzumab-axgb IV	Rate of Infusion
Cycle 1	Day 1	1 mg	Administer over a minimum of 4 hours; note rate may need to be prolonged in any cycle if toxicity occurs (see product labeling)
	Day 8	2 mg	
	Day 15	60 mg	
Cycle 2	Day 1	60 mg	Administer over 2 hours if infusions from Cycle 1 were well-tolerated
Cycles 3+	Day 1	**30 mg***	

*Note dose change from 60 mg to 30 mg for Cycle 3 and beyond, provided no dose delays

Table 2: Recommendations for Restarting mosunetuzumab-axgb after a Dose Delay Due to Toxicity or Other Cause

Last dose administered	Time since last dose administered	Action for next dose(s)
1 mg Cycle 1 Day 1	1 to 2 weeks	Resume planned treatment schedule (2 mg Cycle 1, Day 8)
	Greater than 2 weeks	Repeat 1 mg (Cycle 1 Day 1), then resume planned treatment schedule (2 mg Cycle 1, Day 8)
2 mg Cycle 1 Day 8	1 to 2 weeks	Resume planned treatment schedule (60 mg Cycle 1, Day 15)
	Greater than 2 weeks but less than 6 weeks	Repeat 2 mg (Cycle 1 Day 8), then resume planned treatment schedule (60 mg Cycle 1, Day 15)
	6 weeks or more	Repeat entire step-up schedule: 1 mg (Cycle 1, Day 1), then 2 mg (Cycle 1 Day 8), then 60 mg (Cycle 1, Day 15)
60 mg Cycle 1 Day 15	1 week to less than 6 weeks	Resume planned treatment schedule (60 mg Cycle 2, Day 1)
	6 weeks or more	Repeat entire step-up schedule: 1 mg (Cycle 2, Day 1), then 2 mg (Cycle 2, Day 8), then 60 mg (Cycle 2, Day 15), then 30 mg (Cycle 3, Day 1)
60 mg	3 weeks to less than 6 weeks	Resume planned treatment schedule (30 mg Cycle 3, Day 1)

Cycle 2 Day 1	6 weeks or more	Repeat 1 mg (Cycle 3, Day 1) and 2 mg (Cycle 3, Day 8), then administer **30 mg** (Cycle 3, Day 15)*, then resume planned treatment schedule (30 mg Cycle 4, Day 1)
30 mg Cycle 3+	3 weeks to less than 6 weeks	Resume planned treatment schedule with 30 mg on Day 1 of subsequent cycle
	6 weeks or more	Repeat 1 mg (Day 1) and 2 mg (Day 8), then **30 mg** (Day 15)*, then resume planned treatment schedule with 30 mg on Day 1 of subsequent cycles

* For the Day 1, Day 8, and Day 15 doses in the next cycle, administer premedication for all patients

Table 3: Premedication

Treatment Cycle	Patients Requiring Premedication	Premedication	Dosage	Administration
Cycles 1 & 2	All patients	Corticosteroid	Dexamethasone 20 mg IV or methylprednisolone 80 mg IV	Complete at least 1 hour prior to infusion
		Antihistamine	Diphenhydramine 50 mg-100 mg or equivalent oral or IV antihistamine	At least 30 minutes prior to infusion
		Antipyretic	Oral acetaminophen (500 mg-1,000 mg)	At least 30 minutes prior to infusion
Cycles +3	Patients who experienced any grade CRS with the previous dose	Corticosteroid	Dexamethasone 20 mg IV or methylprednisolone 80 mg IV	Complete at least 1 hour prior to infusion
		Antihistamine	Diphenhydramine 50 mg -100 mg or equivalent oral or IV antihistamine	At least 30 minutes prior to infusion
		Antipyretic	Oral acetaminophen (500 mg-1,000 mg)	At least 30 minutes prior to infusion