HEMATOLOGY-ONCOLOGY ASSOCIATES OF CENTRAL NEW YORK, PC

Department(s): Medical Oncology	**Policy Name / Description:** Management of Bispecific T-cell Engager (BiTE) Therapy - Inpatient
Approved Date:	**Approved By**:
Effective Date:	**Date Retired**:
Version: 1.0	

SCOPE

Outlining the care and management of patients who are admitted for Bispecific T-cell Engager (BiTE) therapy management of CRS/ICANS.

PURPOSE

Definition:

- **Bispecific T-cell Engager (BiTE) therapy:** A subtype of immune effector cell (IEC) therapy which connects the patient's immune system to tumor cells, activating the patient's own natural T cells to kill cancer cells. BiTE therapy does not require collection or engineering of patient's cells. It is designed to overcome cancer cells evasion of the immune system by activating the cryoprotective potential of patient's own T cells to directly target cancer cells.
- **Cytokine Release Syndrome (CRS):** A disorder characterized by fever, tachypnea, headache, tachycardia, hypotension, rash, and/or hypoxia caused by the release of cytokines. Symptoms can be progressive, but always include fever at the onset and may include hypotension, capillary leak syndrome, hypoxia and end organ dysfunction. CRS typically occurs within 1 to 14 days after infusion and typically last 5 to 10 days after infusion.
- **Immune Effector Cell-Associated Neurotoxicity (NT) Syndrome (ICANS):** A disorder characterized by a pathologic process involving the central nervous system following any immune therapy that results in the activation or engagement of endogenous or infused T cells and/or other immune effector cell. Signs or symptoms can be progressive and include aphasia, altered level of consciousness, impaired cognitive skills, motor weakness, seizures and cerebral edema. Can occur concurrently or at separate time from CRS. Higher grade NT is associated with higher grade CRS. Median onset is 2 to 14 days after infusion, usually within 8 weeks and typically last 6 to 21 days after infusion.
- **Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS):** This is a disorder closely associated with severe CRS. It is caused by excessive activation and multiplication of T cells and macrophages. It can be fatal, but the majority of the time symptoms resolved with resolution of CRS.

POLICY & PROCEDURES

- When patient calls or is seen in the office with changes in baseline CRS/ICANS score that are outside of outpatient management parameters, the patient will be directed to the Crouse ED where the on-call oncologist will meet the patient and copy of Bispecific Assessment Tool – Initial will be sent to ED with patient.

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- Oncologist makes ED provider aware of BiTE protocols available on the Internet and hospital-based EMR and will meet patient at Crouse ED to facilitate management.
- Inpatient Pathway Recommendations:
    - Vital signs and assessments:
        i. Every 8 hours if patient is admitted but not to have suspected CRS/ICANS and anytime there is a change in status
        ii. If patient is located on FLOOR or ED with suspected CRS/ICANS, recommend VS hourly x4, followed by every 2 hrs x4, then per MD guidance or hospital protocol and anytime there is a change in patient status.
        iii. Every 1 hour if patient is located in ICU with suspected CRS/ICANS and anytime there is a change in status
    b. Assessment and grading of CRS (see treatment protocol and initiate inpatient order set)
        i. Assess every 8 hours if patient is admitted but not to have suspected CRS/ICANS for change in patient's status
        ii. If patient is admitted with any grade CRS, see CRS treatment protocol (link will be available on HOACNY website) and activate inpatient order set
    c. Assessment and grading of ICANS (see treatment protocol and initiate inpatient order set)
        i. Assess every 8 hours if patient is admitted but not to have suspected CRS/ICANS for change in patient's status or when there is a change in patient's status
        ii. If patient is admitted for any grade ICANS, see ICANS treatment protocol (link will be available on HOACNY website) and activate inpatient order set,
            1. Consider the need for seizure precaution
            2. Place on aspiration precautions for ICANS grade 3 (withhold oral intake of food, fluid and medications)
            3. If patient develops seizures or status epilepticus, call neurologist
            4. If transferred to ICU due to presence of diffuse cerebral edema or raised intracranial pressure, refer to hospital policies as appropriate
    d. Daily Weight
    e. Daily labs and as needed:
        i. CBC, CMP, LDH, uric acid daily and ferritin (prn)
    f. DVT/VTE prophylaxis
    g. Notify oncologist of any of the following:
        i. SBP greater than 140 or less than 90 mmHg
        ii. Heart rate greater than 120 or less than 60 bpm or an arrhythmia
        iii. Respiratory rate greater than 25 or less and 12 breaths/min

iv. Oxygen saturation less than 92% on room air
v. Change in weight > 5 lbs
vi. Upward trend in serum creatinine or liver function test
vii. Tremor or jerking movement in the extremities
viii. Any increase in CRS or ICANS overall grade
ix. Temperature greater than or equal to 100.4 °F.

h. Do not administer corticosteroids unless approved by oncologist/provider
i. PRN tocilizumab to be activated only if directed by oncologist/provider
j. Patients with febrile neutropenia should be worked up for infectious complications as signs and symptoms if infection/sepsis are difficult to delineate from CRS.
    i. Contact oncologist for orders.
    ii. Fever may be managed by acetaminophen. And cooling blankets
    iii. Do not use NSAIDs unless fever is refractory to other measures
    iv. Patients with neutropenia should be placed on neutropenic precautions
    v. Note: Growth factor use within the first 3 weeks after infusion or before CRS resolves is controversial due to concern for macrophage activation increasing the risk for CRS
k. Transfusion and/or growth factor support may be needed to keep hemoglobin ≥ to 8 g/dL, platelets ≥ 20,000 and ANC ≥ 1500. If blood products are ordered, administer according to policy.
l. Thrombocytopenia precaution should be utilized if patient's platelets are 50,000 or less
m. Monitor patient for development of IEC-associated Fulminant Hemophagocytic Lymphohistiocytosis (HLH) and/or Macrophage Activation Syndrome (MAS)
    i. Notify oncologist if patient has a rapidly rising and high ferritin greater than 10,000 ng/mL during the CRS phase and develops any 2 of the following organ toxicities:
        1. Grade 3 or higher increase in bilirubin (3x upper limit of normal), AST/ALT (5x upper limit of normal)
        2. Documented presence of hemophagocytosis by morphology and/or CD68 IHC and bone marrow or organs
        3. Grade 3 or higher oliguria (less than 80 mL of urine output in 8 hours) OR grade 3 or higher serum creatinine level (3x the baseline or 3x upper limit of normal)
        4. Grade 3 or higher pulmonary edema (dyspnea at rest, oxygen indicated)
n. Monitor for tumor lysis syndrome (TLS). Risk is more prolonged than with standard chemotherapy

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i. Patient is not being hydrated, contact oncologist for fluid order
ii. CMP as ordered
iii. Report elevated and/or increasing potassium, phosphate, BUN, creatinine, LDH and uric acid levels to oncologist
iv. Report urine output less than 2 mL/kg/h for any 4-hour period, cloudy urine, nausea, vomiting, shortness of breath, lethargy, irregular heartbeat and or joint discomfort
v. Initiate TLS prophylaxis/treatment orders if directed by oncologist