| [Clinic or Hospital Logo] | | | |
|---|---|---|---|
| | | SOP # | [Number] |
| | | Effective | [Date] |
| | | Approved | [Date] |
| | | Next Review | [Date] |
| | | Owner | [Name] |
| | | Department | [Name] |
| | | Tags | [Tags] |
| | | Applicability | [Name of sites] |

# On-Call Symptom Interventions for Patients Receiving Bispecific T-Cell Engagers

| Where Did This Resource Come From? | |
|---|---|
| Clinic/Hospital Type | Mid-sized, community cancer clinic |
| What's Unique? | • Table with symptoms, differential diagnoses, and recommended workup, management, and monitoring.<br>• This resource is quick reference for on-call providers |

## 1. Purpose

This protocol serves as a reference for managing common patient complaints related to bispecific antibody therapies, providing symptoms, potential causes, and recommended interventions to ensure timely patient care.

## 2. Scope

This policy is applicable to all clinical staff at [site name].

## 3. Definitions

- **Bispecific T-Cell Engager (BTCE)**: Synthetic proteins that bind two distinct antigens: one targets the CD3 protein on T cells, and the other targets a specific cancer antigen, redirecting T cells to activate an antitumor immune response.
- **Step-Up Dose**: A dosing strategy that starts with a lower dose and gradually increases it to effectively prime the immune system while minimizing adverse effects.
- **Cytokine Release Syndrome (CRS)**: A potentially severe inflammatory response that occurs when immune effector cell therapy leads to the release of cytokines into the bloodstream. This syndrome causes symptoms such as fever, hypotension, hypoxia, chills, tachycardia, dyspnea, nausea, rash, headache, and myalgia.

- **Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)**: A neurological complication caused by inflammation in the central nervous system following immune effector cell therapy. Symptoms can range from mild, such as headache and confusion, to severe, including seizures and coma, which may be life-threatening.
- **Neurotoxicity**: Side effects that impact the nervous system, including those caused by immunotherapy.
- **Immune Effector Cell Encephalopathy (ICE) Score**: A clinical scoring tool for assessing the severity of neurological symptoms associated with immune effector cell therapies.

## 4. Symptom-Driven Interventions and Follow-Up

- Table 1 lists potential side effects associated with BTCEs, their interventions, and necessary work up and monitoring.

### Table 1. Management of Potential BTCE-Associated Toxicities

| Symptom | Potential Causes | Intervention | Follow-Up |
|---|---|---|---|
| Fever (≥100.4°F (38°C)) | CRS, infection, tumor lysis syndrome | Grade 1 (Mild CRS): Administer antipyretics (acetaminophen), ensure hydration, monitor vitals.<br><br>Grade 2 (Moderate CRS): IV fluids, consider tocilizumab if CRS suspected, obtain cultures to rule out infection, monitor CRP and ferritin.<br><br>Grade 3 or higher (Severe or Life-Threatening CRS): Escalate care, initiate vasopressors if hypotension occurs, administer tocilizumab or corticosteroids. | Daily monitoring of CRP, ferritin, CBC, and vital signs.<br><br>Consider blood and/or urine cultures, chest X-ray, and IV lines to rule out infection. |
| Headache and Mild Confusion | Early signs of ICANS, dehydration, or medication side effects. | Perform ICE exam to assess cognitive function.<br><br>For Grade 1 (Mild ICANS): Observation, hydrate, provide symptomatic treatment (NSAIDs).<br><br>For Grade 2 or higher: Initiate corticosteroids (dexamethasone), EEG if seizures suspected, and consider ICU evaluation if symptoms worsen. | Recheck ICE score daily, repeat labs (CBC, electrolytes), consider neuroimaging if persistent or worsening symptoms. |
| Shortness of Breath (Dyspnea) | CRS, pulmonary infection, hypoxia, or other underlying pulmonary conditions. | Grade 1-2: Administer supplemental oxygen, monitor SpO2, and check inflammatory markers (CRP, ferritin).<br><br>May also discuss environmental considerations (e.g., avoiding smoking, stimulating the trigeminal nerve through some fresh air, assistive devices (i.e., wheelchair) to decrease physical activity that may worsen dyspnea.)<br><br>Grade 3: High-flow oxygen or non-invasive ventilation, administer tocilizumab if CRS is suspected, consider corticosteroids.<br><br>Grade 4: ICU admission, mechanical ventilation, suctioning or opening of airways; and high-dose corticosteroids. | Serial blood gases, chest imaging (CXR or CT), and continuous SpO2 monitoring. |
| Seizures or Altered Mental Status | ICANS, metabolic imbalances, or CNS infection | Grade 2-3 ICANS: Administer corticosteroids (e.g., dexamethasone), anti-seizure medications (levetiracetam), and consider EEG monitoring. | Continuous EEG, frequent neurochecks (ICE score), and repeat metabolic panels. |

| | | | |
|---|---|---|---|
| | | Grade 4 ICANS: ICU care, mechanical ventilation, high-dose corticosteroids, and potential IL-1 blockade (anakinra).<br><br>Ensure correction of electrolyte imbalances (e.g., sodium) and monitor closely for cerebral edema (via neuroimaging if necessary). | |
| Hypotension | CRS, sepsis, or dehydration | Grade 1-2: IV fluids (crystalloid), monitor for response to fluids, and reassess inflammatory markers.<br><br>Grade 3: Administer vasopressors (norepinephrine) if hypotension persists despite fluids, initiate tocilizumab and corticosteroids if CRS suspected.<br><br>Grade 4: ICU transfer for vasopressor support, continuous hemodynamic monitoring, and high-dose steroids. | Serial CBC, electrolytes, renal function, and CRP/ferritin levels. |
| Chest Pain (Angina) | CRS-related cardiac involvement, myocardial ischemia, or anxiety | Evaluate ECG and cardiac enzymes (troponin).<br><br>Administer oxygen, nitroglycerin (if ischemic symptoms), and initiate IV fluids.<br><br>Consider echocardiogram if CRS suspected to assess for myocardial involvement.<br><br>For significant cardiac findings: Initiate corticosteroids and transfer to ICU for further management. | Continuous ECG monitoring, repeat cardiac enzymes, and inflammatory markers. |
| Severe Abdominal Pain | CRS, gastrointestinal infection, or tumor lysis syndrome | Check for signs of organ dysfunction (liver, renal markers).<br><br>Administer analgesia and fluids, and consider corticosteroids if CRS is suspected.<br><br>Obtain abdominal imaging (CT scan) and consider surgical evaluation if necessary. | Monitor liver function tests (LFTs), renal function, and abdominal pain progression. |
| Severe Fatigue or Malaise | CRS, anemia, dehydration, or electrolyte imbalance | Grade 1-2 CRS: Symptomatic care, encourage hydration, and monitor CBC and electrolytes.<br><br>Grade 3 or higher: Escalate care with IV fluids, consider corticosteroids, and evaluate for anemia or electrolyte disturbances. | Recheck CBC, CRP, and electrolytes regularly |
| Rash or Skin Changes | Immune-related dermatitis, drug reactions, or CRS | Administer topical corticosteroids and antihistamines for mild reactions.<br><br>If widespread or severe: Consider systemic corticosteroids and consult dermatology. | Monitor for systemic involvement (e.g., mucosal involvement or fever) and escalate care if needed. |

Abbreviations: CBC, complete blood count; CRP, C-reactive protein; CRS cytokine release syndrome; CT, computed topography; CXR, chest X-ray; ECG, electrocardiogram; EEG, electroencephalogram; ICANS, immune effector cell associated neurotoxicity; ICE, immune effector cell encephalopathy; ICU, intensive care unit; SpO2, oxygen saturation

## General Follow-Up:

- **Daily ICE score** for patients with neurological complaints.
- **Daily labs** including CBC, CRP, ferritin, electrolytes, renal and liver function for patients with CRS.
- **Close monitoring** of vital signs (heart rate, SpO2, blood pressure) for patients experiencing respiratory, cardiac, or hypotensive symptoms.
- Instruct patients/caregivers to report any new neurologic symptoms immediately, even between visits

## 5. Revision History

| Version # | Date | Description of Changes | Reviewed / Approved By |
|---|---|---|---|
| | | | |
| | | | |
| | | | |
| | | | |