

ASSOCIATION OF  
COMMUNITY  
CANCER CENTERS

Best practices in expanding  
access to  
**BISPECIFIC  
ANTIBODIES  
AND  
ADVERSE EVENT  
MANAGEMENT**

Issues Brief

## INTRODUCTION

**B**ispecific antibodies (BsAbs), an emerging class of novel immunotherapy agents, have great therapeutic potential; however, they also present barriers to care including unique and serious treatment-related toxicities.<sup>1</sup> These, and other practical administration considerations, can limit the widespread use of BsAbs in the community oncology practice setting. Beginning in 2020, the Association of Community Cancer Centers (ACCC) initiated research and education focused on the utilization of BsAbs in the community oncology setting. Findings from an ACCC survey illuminated several barriers to using BsAbs in the community setting.<sup>2</sup> Among these, 59% of survey respondents indicated that they have experienced barriers when caring for patients treated with BsAbs.

### Common challenges cited include:

- Transitioning patients from the inpatient to outpatient setting (41%)
- Managing patients in remote areas (33%)
- Securing insurance coverage (28%)
- Managing side effects (27%)
- Assisting patients with treatment costs (24%)
- Lacking in-house expertise with the drug class (22%)

ACCC also released a “Bispecific Antibodies Checklist” that reminds community providers to review any Risk Evaluation and Mitigation Strategy (REMS) program details, educate staff about side effects, create treatment algorithms for toxicity management, and clearly outline which parts of treatment will be handled by the community cancer program vs. an academic or tertiary care center.<sup>3</sup>

In 2022, ACCC launched a new project which builds upon its previous work titled, “Best Practices in Expanding Access to Bispecific Antibodies and Adverse Event Management.” This educational project explores ways to expand patient access to BsAbs and identify methods to optimize the early identification and management of treatment-related adverse events (TRAE) with a focus on cytokine release syndrome (CRS).

## FOCUS GROUP

In part with this initiative, in August 2022, ACCC held a focus group to explore how cancer programs are managing TRAE in patient-treated with BsAbs that engage T-cells. The focus group also included discussions around care coordination and some of the challenges associated with co-managing patients between a community cancer program and an academic or tertiary medical center.

### As of September 2022, the FDA-approved BsAbs that engage T-cells include:

- Blinatumomab (BLINCYTO) for CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL)
- Tebentafusp-tebn (KIMMTRAK) for uveal melanoma

Both agents have a boxed warning for CRS. BLINCYTO also has a REMS program that covers CRS, neurological toxicities, and preparation and administration errors.<sup>4</sup>

Examples of a few investigational BsAbs that engage T-cells include talquetamab for multiple myeloma, mosunetuzumab for non-Hodgkin’s lymphoma, and epcoritamab for diffuse large B-cell lymphoma.<sup>5</sup>

## TREATMENT SETTINGS

### When considering the treatment framework for patients treated with BsAbs, most receive care in one of the following settings:

- **Scenario 1:** Patient is diagnosed and treated with BsAbs at an academic or tertiary care center. Follow-up care is coordinated through the same institution.
- **Scenario 2:** Patient is diagnosed in the community setting and seen by a local oncologist. The patient is referred for BsAbs treatment at an academic or tertiary care center. After treatment begins, follow-up care occurs with the local oncologist or is co-managed between the local oncologist and the treatment center.

In Scenario 2, there is a need to clearly define how patients should be managed once they leave the treatment center. If the patient travels back home after receiving treatment, a local hospital may need to provide care for certain treatment-related reactions. In some cases, the patient may begin treatment at the academic center and then return home to continue ongoing treatment with a local oncologist. During the focus group, participants explored ways to improve the coordination around these important elements.

## TREATMENT INITIATION

Focus group participants indicated that most patients are started on BsAbs in the inpatient setting to watch and monitor patients closely for signs of serious adverse reactions. As many hospitals administering BsAbs also have stem cell transplant units and experience administering chimeric antigen receptor (CAR) T-cell therapy, their clinicians are trained and equipped to manage patients who may develop serious adverse reactions. Currently, BsAbs are used to treat a few cancers; as such, hospitals have the capacity to hospitalize these patients during treatment initiation. However, if

the use of BsAbs expands to treat more types of cancers, inpatient administration would not be feasible for every new patient who begins therapy.

When patients are treated with BsAbs, insurance-related administrative work (e.g., prior authorizations, approvals, etc.) is time-consuming, but financial advocates have helped patients through these processes tremendously. As patients often qualify for co-pay assistance and other programs, hospitals offering BsAbs should proactively check to see which patients may be eligible.

## COORDINATING REFERRALS AND FOLLOW-UP CARE

As the use of BsAbs expands in the community, there is a need to improve the coordination of referrals and follow-up care if patients receive treatment outside of their local community. Trusted partnerships between academic medical centers and referring community cancer programs are needed to ensure smooth patient referrals and seamless follow-up care as patients travel for treatment and return home.

### During the focus group, participants provided the following suggestions to ensure optimal care coordination:

- Establish strong relationships between clinicians working at academic and community cancer programs. Build on existing referral pathways (e.g., for stem cell transplant or clinical trials) and ensure that office staff are familiar with the referral process.
- Create an online resource (e.g., cellulartherapies.com) to help prepare patients to receive treatment initiation at an academic medical center and follow-up care with a local oncologist. The website can guide patients through the process and help them understand what to expect.
- Use telehealth to provide follow-up care, monitor for symptoms, and coordinate with local providers for patients who live further away from academic or tertiary care centers.
- Connect patients with navigators who know how to coordinate logistics between community cancer programs and academic medical centers, if available. While many community cancer programs have navigators for common cancers, they may not have navigators for some of the less common hematologic malignancies.
- Create a patient information sheet that clearly outlines team members and their roles and responsibilities across the different sites of care (e.g., community cancer program, local hospital, academic medical center, etc.).

## CYTOKINE RELEASE SYNDROME (CRS)

To reduce the risk of CRS, BsAbs are usually administered using step-up dosing. While most BsAbs are administered as infusions, some investigational agents are administered subcutaneously. Focus group participants indicated that while they often see CRS in patients who have been treated with BsAbs, symptoms tend to be relatively mild (often grade 1 or 2) and appear to resolve quickly after patients receive steroids and/or treatment with tocilizumab. While some hospitals have a protocol that enables physicians to treat grade 1 CRS in the outpatient setting, patients with grade 2 and above are automatically admitted.

The National Comprehensive Cancer Network (NCCN) Guidelines for the Management of Immunotherapy-Related Toxicities includes a section on CRS for patients treated with CAR T-cell therapy but does not include a section on CRS from BsAbs.<sup>6</sup> Similarly, the American Society of Clinical Oncology (ASCO) supportive care guidelines that address CRS are also specific to CAR T-cell therapy.<sup>7</sup>

BsAbs have a relatively shorter half-life and need to be administered repeatedly, therefore CRS symptoms tend to resolve relatively quickly by interrupting therapy and providing supportive care.<sup>8</sup> As more BsAbs enter the market, researchers and clinicians may find better ways to prevent and manage CRS associated with BsAbs.

### The following are ideas and themes that emerged during the focus group around improving the management of CRS in patients treated with BsAbs:

- Ensure emergency department staff and hospitalists are aware that an on-call physician is available to help manage any patient who may present with CRS.
- Develop a structured training program for staff. Include hospital nurses, ICU staff, and neurologists in conversations about CRS and neurotoxicity.
- Develop a central repository of treatment protocols and algorithms, including toxicity management plans. Share these with local community hospitals (and those in the cancer program network) to ensure that a consistent approach is delivered wherever the patient is treated.
- Remind patients and their caregivers about signs and symptoms of CRS. Caregivers may be the first ones who recognize symptoms and should be prepared to call the cancer care program for assistance.

### Focus group participants also acknowledged that several important questions remain difficult to answer at this time and require further consideration:

- What happens if a patient returns home, develops CRS, and is treated at a local hospital that is not equipped to handle CRS? While the patient may be transferred to a tertiary hospital, what infrastructure and pathways can the local hospital have in place to be properly equipped? Many hospitals continue to face staffing shortages and other factors that may limit how much care certain hospitals can provide.
- How can hospitals assess whether they are adequately staffed and equipped to offer BsAbs and manage potential TRAE like CRS? Many of the current hospitals that offer BsAbs have transplant programs and/or experience with CAR T-cell therapy, so their care teams are experienced in managing CRS.

### FUTURE DIRECTION

Additional BsAbs are likely to emerge to treat a wide variety of cancers, including solid tumors.<sup>9</sup> Community cancer programs need to be prepared to navigate the complex landscape of treatment initiation, adverse event management, and follow-up care. While CRS can be serious, mild cases are being managed safely and effectively as clinicians identify symptoms early and provide the right interventions. ACCC will post updates and resources on its website [Best Practices in Expanding Access to Bispecific Antibodies and Adverse Event Management \(accc-cancer.org\)](https://www.accc-cancer.org) as it continues to explore ways to improve the coordination of patient referrals and follow-up care after treatment initiation of BsAbs.

### ACKNOWLEDGEMENTS

Thank you to those who participated in the ACCC Focus Group on August 5, 2022.

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Thank you to our project sponsor, Janssen Oncology.



A publication from the ACCC education program, "Best Practices in Expanding Access to Bispecific Antibodies and Adverse Event Management." Learn more at [accc-cancer.org/expanding-access-BsAbs](https://www.accc-cancer.org/expanding-access-BsAbs).

**The Association of Community Cancer Centers (ACCC)** is the leading education and advocacy organization for the cancer care community. For more information, visit [accc-cancer.org](https://www.accc-cancer.org).

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