

Readiness for Bispecific Antibody Therapy: Initiation and Maintenance Phases

INTRODUCTION

Over the last 2 decades, the development of bispecific antibodies (BsAbs) has revolutionized cancer treatment.¹ Developed to address drug resistance and to improve treatment safety and efficacy, bispecific antibodies have 2 distinct binding domains that can bind to 2 antigens or epitopes simultaneously. Although BsAbs are a promising new therapeutic approach, especially for hematologic malignancies in the relapsed/refractory settings, BsAbs are associated with adverse effects such as cytopenias, diarrhea, transaminitis, and tumor lysis syndrome, as well as cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and tumor flare.²

Opportunities exist to expand the adoption of BsAbs. Community oncology practices, which serve the majority of patients with cancer, are uniquely positioned to administer these innovative treatments and enhance patient outcomes.

The Association of Cancer Care Centers (ACCC) in partnership with the Lymphoma Research Foundation (LRF) and the Advanced Practitioner Society for Hematology and Oncology (APSHO) developed an educational initiative, which aimed to prepare multidisciplinary cancer care teams for the successful integration of BsAbs into community oncology settings and to help care teams assess readiness for the safe administration of BsAbs.

To support this effort, ACCC developed a set of resources for providers to use when planning to treat patients with BsAbs. Below is a summary of key insights, gathered from a landscape analysis and focus group discussions, that highlight best practices for the ramp-up and maintenance phases of BsAb therapy.

LANDSCAPE ANALYSIS HIGHLIGHTS



Financial Affordability and Sustainability

Cancer care may create financial hardship for patients. It is critical for the cancer care team to assess needs throughout the care journey, connecting patients and their caregivers with team members who can help to navigate financial barriers and identify available financial assistance programs.

Novel innovative therapies are often not fully covered by insurance providers and in some cases, may not be covered at all. Provider organizations should establish a process to verify benefits and secure any necessary prior authorizations. This ensures potential barriers or coverage gaps for BsAbs and supportive care medications are identified early and addressed promptly, minimizing any treatment delays.



Patient and Caregiver Education and Engagement

Patients and caregivers must be informed about the potential adverse events related to BsAb treatment. Education should review strategies for preventing toxicities and how symptoms will be managed if they occur. Useful resources include patient wallet cards, emergency contact numbers, and a list of symptoms to monitor. Equally important is ensuring that cancer care team members stay up to date on the latest recommendations and guidelines for preventing and managing toxicities that may result from BsAb treatment.

Key principles include promoting health literacy, enhancing patient navigation, and supporting remote patient monitoring.



Adverse Event Management

Recent studies of treatment-related adverse events for bispecific antibodies demonstrate:



the prevalence of infections was 35%



neutropenia occurred in 31% of patients



CRS occurred in 45% of patients



neurotoxicity or ICANS was observed in 12% of patients.³

Resources are available to support providers with adverse event management, such as commentaries, blogs, and other publicly available sources such as LRF consensus recommendations,⁴ International Myeloma Working Group consensus guidelines,⁵ or the National Comprehensive Cancer Network Guidelines®



Operational Considerations

To ensure consistent care coordination, cancer centers should establish clear workflows for managing adverse events, particularly when determining hospital admission versus outpatient care and during care transitions (such as transition from academic center for ramp-up to community center for maintenance). For example, depending on the BsAb used, hospitalization may be recommended or required due to the potential for certain toxicities.

Care providers should focus on key operational considerations: implementing policies and procedures for risk evaluation and mitigation (REMS), utilizing order sets and acute care plans, and providing ongoing training and education to keep providers informed of the latest information about BsAbs

INSIGHTS FROM FOCUS GROUPS

In June 2024, ACCC held focus groups to capture insights, barriers, challenges, best practices and solutions regarding the use of BsAbs. ACCC conducted 2 focus groups that included participation from 30 multidisciplinary cancer care professionals.

Focus groups were designed to promote clinical awareness of BsAbs, reinforce the potential for application in the community setting, and discuss the practical and financial considerations of care delivery. The discussion also focused on supportive care needs related to adverse event management and patient triage, as well as strategies for developing a robust referral network. This includes patient navigation, defining internal roles and responsibilities, establishing business agreements, and streamlining logistical processes.

There were 7 key categories examined during focus group discussions, including:

- Common misconceptions and barriers
- Phases of administration
- Readiness for implementation
- Capacity building and infrastructure
- Financial affordability and sustainability

- Adverse event management
- Provider education.

Detailed information about the focus group findings is outlined below.

Common Misconceptions and Barriers

Focus group participants identified several misconceptions, including the belief that BsAbs are the same as chimeric antigen receptor (CAR) T-cell therapy, confusion about the incidence of BsAb-related adverse events during ramp-up versus maintenance therapy, and the assumption that patients consistently do well while receiving BsAbs. They also highlighted barriers to care, such as limited awareness of where BsAbs fit into treatment plans. Additionally, participants noted a general hesitancy and fear among providers, stemming from unfamiliarity with the BsAb toxicity profile and care management—essentially, a fear of the unknown.



“The biggest misconception I’ve faced has been from leaders outside of our oncology service line [who are] really just struggling to understand...the place in therapy of these products, and the fact that this is something we’re going to be seeing more and more frequently in coming years.”

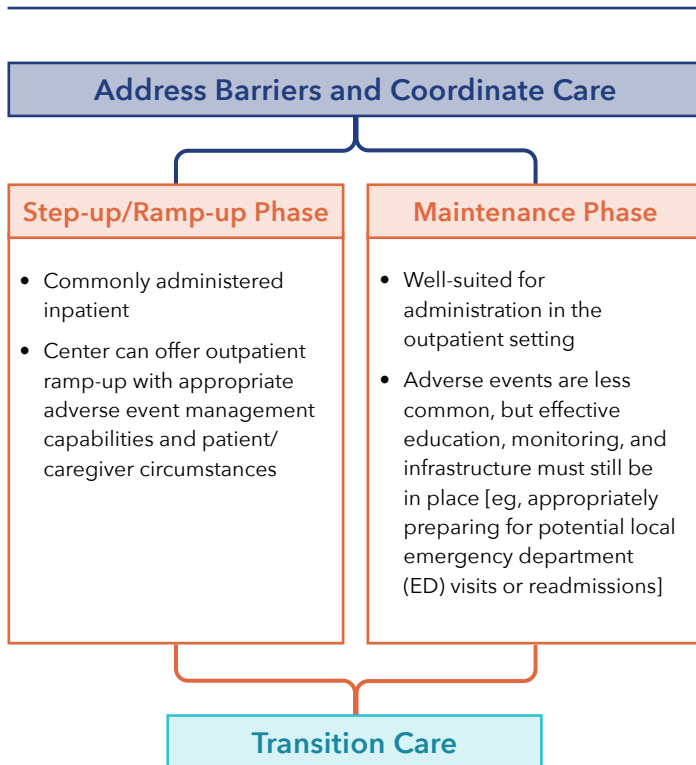
— Focus Group Participant



Phases of Administration

Focus group participants emphasized the need for cancer centers to consider the different capabilities necessary for the initiation (ie, ramp-up) phase compared to the maintenance phase. Effective cross-organizational coordination is needed to remove barriers and safely transition patient care closer to (or at) the patient’s home. Specifically, there is concern about the division of care responsibilities between treatment locations during different phases of care. Some institutions will admit patients to the hospital during the ramp-up phase and for the beginning of maintenance therapy (see **Figure 1**).

Figure 1. Focus Group Definition of Phase Administration



“We are a small, rural, multi-hospital health system and are currently in a phase where we’re being asked by larger institutions if we’re able to take care of their [patients] closer to home. We’re in the investigating phase—what our limitations are, what our needs are, and things we need to work on.”

— Focus Group Participant

Readiness for Implementation

While focus group participants agreed that BsAbs will become a cornerstone of oncology treatment, there was a general awareness and acceptance that not all cancer centers have equal capacity for administration. Focus group participants shared their levels of experience with BsAbs, which ranged from academic

centers that have both clinical trial and real-world experience to centers that are experienced with the maintenance phase but are exploring ramp-up capabilities. Other centers do not currently offer BsAbs but are interested in learning more.

Capacity Building and Infrastructure

Administrators, hospitalists, physicians, nurses, pharmacists, financial advocates, and manufacturer medical science liaisons (MSLs) all play a role in capacity building for cancer centers.

Recommendations from focus group participants for effective capacity and infrastructure building include:

- Assess your center’s capabilities and use that information to hone patient and caregiver criteria needed to treat patients safely (eg, transportation and lodging options).
- Develop a playbook for each medication, including care coordination, adverse event management, acquiring and handling specific drugs, and prior authorization.
- Take a multidisciplinary approach to building ramp-up and maintenance-specific algorithms.
- Use academic programs and manufacturers as resources to support building out your BsAb capabilities.
- Start with 1 BsAb drug and build out from there; it is not feasible for all community programs to offer every approved BsAb immediately.

Financial Affordability and Sustainability

Insurance-related administrative tasks (eg, prior authorizations, approvals) for BsAbs can be time-consuming. A multidisciplinary team comprised of financial advocates and navigators, administrators, billing and prior authorization staff, physicians, social workers, and manufacturers can support patients through these barriers to care.

Recommendations from focus group participants include:

- Determine how to structure prior authorizations (ie, separate inpatient and outpatient).
- Establish a path for coverage if a patient starts as an inpatient and transitions to being an outpatient.
- Have a process in place to submit appeals while the J code (drug billing code) is still being established.
- Refer to manufacturer references and guidelines for treatment authorization.

- Leverage copay and foundation assistance, manufacturer programs, and other resources to help cover drug costs as well as other needs, like transportation or housing.

Adverse Event Management

There are common adverse events associated with BsAb therapy, such as CRS, infections, and neutropenia. To prevent and rapidly treat adverse events, the multidisciplinary care team must implement effective patient and caregiver in-home assessments and remote monitoring capabilities.

Recommendations from focus group participants include:

- Build out electronic health records.
- Establish clear criteria for patient/caregiver selection for outpatient administration.
- Implement processes for training and contacting caregivers to check in with patients (eg, triage team follow-up), particularly if BsAbs are delivered in the outpatient setting.
- Create clear and open lines of communication between programs (eg, provision of progress notes, discharge summary and transition of care notes, sharing direct contact information of individual contacts at the ramp-up site, maintenance site, and local emergency department).

Provider Education

Focus group participants highlighted the importance of multidisciplinary team member education that includes the most up-to-date information about BsAb initiation and maintenance. Educational materials should be developed with the audience in mind, which could include physicians, advanced practice providers, nurses, pharmacists, case managers, social workers, patients, and caregivers.

Recommendations from focus group participants include:

- Establish an authorized representative to lead risk evaluation and mitigation strategy (REMS) training and certification requirements.
- Educate the team about the clinical nuances of each drug.
- Make recordings of education available for staff to view on demand.
- Use MSLs as a resource; have them visit on site to provide drug-specific training to both inpatient and outpatient teams.
- Ensure a broad multidisciplinary approach to provider training.

KEY TAKEAWAYS AND RECOMMENDATIONS

- 1 **Key challenges** exist that limit the delivery of BsAbs outside of academic settings. These novel therapeutics require specialized handling, administration, and monitoring to ensure safety. Cost is another challenge—BsAbs can be expensive, and community practices may face reimbursement challenges that impact their ability to offer these treatments to patients.

Despite these challenges, community oncology practices play a critical role in delivering BsAbs to patients. By collaborating with academic centers, pharmaceutical companies, and other stakeholders, community practices can access the necessary resources and support to offer these innovative therapies to their patients.

- 2 **Capacity building** is a crucial aspect to consider in the context of delivering BsAbs, particularly in community oncology practices. Capacity building includes strengthening the skills, knowledge, resources, and infrastructure of health care providers to effectively deliver BsAbs to patients.

One key aspect of capacity building is training and education. Health care professionals—including oncologists, nurses, pharmacists, and other staff members—may require specialized training to understand the unique mechanisms of action, administration procedures, and monitoring requirements. In addition, investing in infrastructure and resources to support BsAb delivery is important. This may include upgrading facilities to accommodate the storage and administration of these therapies, as well as implementing systems for monitoring and managing potential adverse effects.

- 3 **Increased awareness** is necessary to educate patients and the broader health care community about the therapeutic potential for BsAbs in oncology. Fostering greater understanding and engagement can help ensure that patients have access to the latest advances in cancer treatment and are empowered to make informed decisions about their care. Stakeholders, including policymakers, health insurers, and industry partners, should collaborate to address barriers to the widespread adoption of BsAbs in oncology. This may involve advocating for improved reimbursement policies, supporting the development of guidelines for the use of these therapies, and cultivating a collaborative ecosystem that promotes innovation and access to cutting-edge treatments.

CONCLUSION

Bispecific antibodies offer an exciting treatment opportunity to the cancer community and, specifically, patients with cancer. The findings of the focus groups and landscape analysis underscore the role of BsAbs in transforming cancer care. By taking action to address barriers, build capacity, raise awareness, and embrace collaboration, cancer care providers can accelerate the integration of these promising therapies into clinical practice and improve outcomes for patients with cancer.

REFERENCES

1. Center for Drug Evaluation and Research. Bispecific antibodies: an area of research and clinical applications. U.S. Food and Drug Administration. Accessed August 28, 2024. [fda.gov/drugs/spotlight-cder-science/bispecific-antibodies-area-research-and-clinical-applications](https://www.fda.gov/drugs/spotlight-cder-science/bispecific-antibodies-area-research-and-clinical-applications)
2. Chennapragada SS. Bispecific antibody toxicity. StatPearls. April 20, 2024. Accessed August 28, 2024. [ncbi.nlm.nih.gov/books/NBK603709](https://www.ncbi.nlm.nih.gov/books/NBK603709)
3. Liu AJ, et al. Prevalence of adverse events following bispecific antibody therapy in non-Hodgkin lymphoma: a meta-analysis. *JCO* 42, e19008-e19008(2024). doi:10.1200/JCO.2024.42.16_suppl.e19008
4. Crombie JL, Graff T, Falchi L, et al. Consensus recommendations on the management of toxicity associated with CD3xCD20 bispecific antibody therapy. *Blood*. 2024. 143(16):1565-1575. doi:10.1182/blood.2023022432
5. Rodriguez-Otero P, Usmani S, Cohen AD, et al. International Myeloma Working Group immunotherapy committee consensus guidelines and recommendations for optimal use of T-cell-engaging bispecific antibodies in multiple myeloma. *Lancet Oncol*. 2024;25(5):e205-e216. doi:10.1016/S1470-2045(24)00043-3
6. Janakiram M, Krishnan A. Bispecific antibodies in refractory multiple myeloma: basics and unanswered questions. ASCO Daily News. March 22, 2023. Accessed August 30, 2024. daily-news.ascopubs.org/do/bispecific-antibodies-refractory-multiple-myeloma-basics-and-unanswered-questions

In partnership with:



Advanced Practitioner
Society for Hematology
and Oncology



Explore additional resources on Bispecific Antibody at acc-cancer.org/BsAbs-Community.

The Association of Cancer Care Centers (ACCC) provides education and advocacy for the cancer care community. For more information, visit acc-cancer.org.

© 2024. Association of Cancer Care Centers. All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means without written permission.

This project is made possible by support from:

