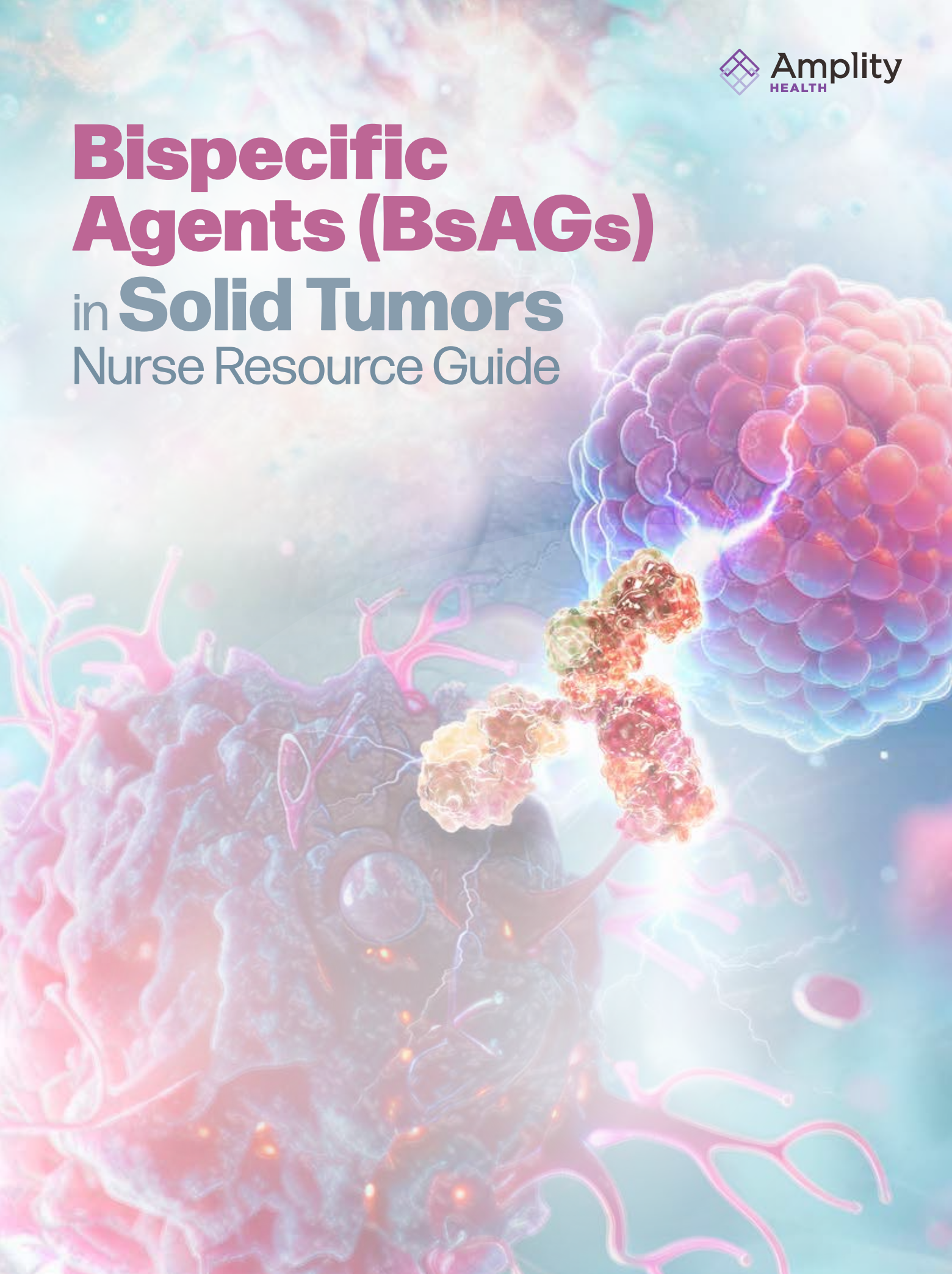
Amplity HEALTH

Bispecific Agents (BsAGs) in Solid Tumors

Nurse Resource Guide



ACADEMY OF ONCOLOGY NURSE & PATIENT NAVIGATORS: MISSION AND VISION

The mission of the Academy of Oncology Nurse & Patient Navigators (AONN+) is to advance the role of patient navigation in cancer care and survivorship care planning by providing a network for collaboration and development of best practices for the improvement of patient access to care, evidence-based cancer treatment, and quality of life during and after cancer treatment. Cancer survivorship begins at the time of cancer diagnosis. One-on-one patient navigation should occur simultaneously with diagnosis and be proactive in minimizing the impact treatment can have on quality of life. In addition, navigation should encompass community outreach to raise awareness targeted toward prevention and early diagnosis, and must encompass short-term survivorship care, including transitioning survivors efficiently and effectively under the care of their community providers.

The vision of AONN+ is to increase the role of and access to skilled and experienced oncology nurse and patient navigators so that all patients with cancer may benefit from their guidance, insight, and personal advocacy.

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AONN+ would like to acknowledge the efforts and dedication of the contributing faculty, who dedicated their knowledge, time, and efforts to enhance the care of patients with cancer through the development of this guide.

The endorsement mark certifies that the information presented in educational seminars, publications, or other resources is reliable and credible.

BsAGs in Solid Tumors Nurse Resource Guide

Introduction

As treatment in solid tumors evolves, therapeutic administration and management strategies are becoming increasingly complex. Bispecific agents (BsAGs), also known as T-cell engagers, bispecific antibodies, or bispecific T-cell engagers, are a novel form of immunotherapy that works by redirecting T cells to tumor cells, harnessing the power of the immune system to induce tumor cell lysis. It is crucial for optimal patient safety and outcomes that prescribers and administration staff be educated on how to properly utilize these agents. This guide, informed by a roundtable discussion of expert nurses, will serve as a resource for both nursing and other medical professionals on how best to begin using BsAGs for solid tumors in the healthcare practice, administration of bispecific agents, as well as monitoring and adverse event management.

Integrating BsAGs into Solid Tumor Clinical Practices

BsAGs represent a novel treatment option for solid tumors. BsAGs require a coordinated and highly specialized multidisciplinary approach to effectively integrate them into clinical practice. These therapies require specific safety protocols for administration and monitoring, representing a large financial investment on the part of the healthcare system in both the acquisition of the drug and training of staff on appropriate use. This section, informed by current literature and an expert nurses' panel, outlines some key considerations for integrating BsAGs into your organizational and clinical workflows.

Identification of Practice and Hospital Champions

The successful launch of BsAGs requires organizational commitment to build an infrastructure for drug acquisition, dispensing, staff training, and implementation. Beyond preparation and delivery of these agents, operational challenges such as electronic health record (EHR) configuration and nurse education must be addressed. Identifying the right practice champion familiar with practice analysis and implementing change is critical to a successful launch. The ideal practice champion should possess:

- **Role:** A practice champion may be a physician, advanced practice provider (APP), pharmacist, registered nurse, or any other individual the organization believes will facilitate a successful and easy launch of BsAG use
- **Clinical experience administering BsAGs:** A champion with clinical experience in administering BsAGs and managing associated side effects will facilitate the smooth development of administration protocols and will gain greater buy-in from the healthcare center
- **Operational and management expertise:** Integration of BsAGs for solid tumor use will necessitate numerous BsAG-specific adaptations in operational and logistical workflow, including enhancements to patient education and monitoring, changes to the EHR system, educating the bedside nurse in identifying and reporting side effects to the team, and staff training. A champion with experience in

implementing similar changes will be well suited to lead this effort. A practice champion should have a deep understanding of clinical and operational aspects of bispecific therapy, be able to identify and influence stakeholders, and invest the time necessary for a successful launch. They should also bear responsibility for creating and updating standard operating procedures, institutional guidelines, or clinical workflows, and ensuring competency for key clinical and administration stakeholders

- **Experienced network:** Bispecific agents are novel in the solid tumor space and represent one of the most complex cancer treatment strategies today. However, BsAGs have been utilized in the hematology space for some time now, and there exists a wealth of knowledge from staff utilizing BsAGs for hematological malignancies. A practice champion with an established network of professionals familiar with the administration of bispecific therapies will provide a resource to integrate best practices and problem-solve for potential barriers or unexpected patient outcomes

Development of a BsAG for Solid Tumor Treatment Plan

The complexity of bispecific treatments necessitates an optimal treatment plan involving the entire care team. Treatment plans may differ slightly for individual organizations, but, generally, involve the following components:

- **Patient selection:** Ensuring the patient meets eligibility for treatment and will benefit from BsAGs, screening for cancer type, stage, mutational status and current or previous lines of treatment if applicable, overall medical condition, and caregiver support
- **Risk evaluation and mitigation strategies (REMS) and logistical considerations:** Verifying the patient is appropriate for BsAG therapy, application of the product-specific REMS protocol (if applicable), obtaining patient consent, confirming site of service (inpatient/outpatient), obtaining insurance authorization, and coordinating scheduling, including inpatient bed reservation (if applicable)

- **Patient and caregiver education:** This should include a detailed schedule, the number and duration of infusions, infusion processes, potential need for hospitalization, rationale for in-person caregiver access and education, provision of a patient wallet card detailing their treatment for other healthcare staff, and contact information for appropriate personnel to report symptoms
- **Pretreatment:** Includes conducting baseline testing of key lab values (complete blood count with differential, liver and kidney function tests, etc), administering baseline immune effector cell-associated encephalopathy (ICE) assessment using appropriate tools, review of treatment orders including initial and step-up dosing, planning for administration of appropriate premedications, and review of appropriate monitoring requirements to promptly identify and mitigate adverse events (AEs) and the risk of serious AEs
- **Dosing and administration (per institutional protocols):** Includes ensuring appropriate venous access for administration, duration, and schedule of treatment; obtaining baseline vital signs before premedication administration; and monitoring for cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). BsAG administration should occur per the product-specific package insert. Aspects that will differ on an agent-by-agent basis include:
  - Necessity of and administration of premedications
  - BsAG administration as per institutional protocol in line with product prescribing information
  - Providing patient and caregiver education on signs and symptoms of potential AEs, strategies for monitoring and management, and which symptoms require emergent reporting and management. All administration and education processes should be documented in the EHR
- **Follow-Up and patient monitoring:** Includes providing patients with a detailed schedule of follow-up appointments. Regular follow-up visits and appropriate laboratory testing (complete blood count with differential, complete metabolic panel, kidney and liver function tests, etc) should be based on the phase of treatment and as outlined in the prescribing information, institutional protocols, and individual patient requirements to ensure efficacious treatment. Clinical staff will need to ensure orders are in place for required laboratory evaluation following drug administration

Creation of Adverse Event Monitoring and Management Protocol

AE management is a key component of administering BsAGs, and requires a plan of action to identify, mitigate, and resolve these events. Having an AE-focused clinical protocol in an easily accessible location that provides detailed descriptions of common BsAG-related symptoms, Common Terminology Criteria for Adverse Events (CTCAE; grades 1-4), or the American Society for Transplantation and Cellular Therapy (ASTCT) grading; and guidelines for monitoring, including warning signs and appropriate clinical steps to manage each AE, will help to prepare clinical staff in early identification and management. Particular attention to CRS and ICANS, unique to BsAGs, should be among the first protocols developed for any institution utilizing BsAGs. Building common AE management medication orders for agents, such as tocilizumab, into the BsAG electronic order set can improve the timeliness of interventions. Providing guided, click-through, menu-based grading criteria for staff to utilize when CRS/ICANS is suspected may aid in standardizing the evaluation of these symptoms, and reduce time to initiating management strategies for the AE.

Development of a dedicated team for cellular therapies, including BsAGs, may be an option for selected practices. This team would consist of highly trained and specialized personnel to ensure that a patient on a BsAG is receiving all the safest and necessary care. This team should have a deeper understanding of the treatment algorithms associated with BsAG therapy, premedications, optimal hydration, and monitoring and management of patients receiving BsAG therapies.

Customized Training for Solid Tumor Care Team Members

With the use of bispecific agents requiring the expertise of the entire care team, training must be tailored to the role of individual team members. Generally, any team member involved in the prescribing, administration, monitoring, or care coordination of patients treated with BsAGs will need training. Team members that may need training include:

- Oncologists
- APPs
- Hospitalists
- Outpatient infusion and inpatient nurses
- Nurse navigators
- Clinical support staff such as medical assistants, pharmacists, emergency department (ED) providers, and other relevant staff

Customized training

For example, BsAG training tailored to nurses may include a greater focus on administration (agents that are intravenous vs subcutaneous), recognizing signs of CRS and ICANS, and initial monitoring. Conversely, a pharmacist's training may focus on optimal dosing for special populations. Providers (physicians and APPs) may be more focused on patient selection and screening, prescribing, and follow-up evaluation of the patient receiving BsAGs.

Staff training should strike a balance between being informative and overexplaining. It is not necessary to provide all the training at once or in a single format. This panel suggested varied formats with a sequenced approach and keeping initial trainings brief, lasting approximately 20 minutes to maximize engagement and attention. Training may be delivered via learning modules, educational videos, and live via nurse educators or physicians. The key is to provide maximal information in an easily digestible manner and provide regular refreshers to keep team members competent. The frequency and modality of refreshers depends on the organization and staff changes, but they should be regular enough to ensure that team members maintain current knowledge while incorporating new information on the therapy as it is released.

Beyond training, there are several supportive resources necessary to ensure safe and effective administration of BsAGs. Nursing AE and treatment plan checklists, appropriate administration and AE management protocols, readily accessible information resources, and appropriate yet not excessive EHR alert prompts are key to ensuring the drug can be safely and easily administered to a patient.

Administration of BsAGs

BsAGs can be one of the most complex therapies a healthcare team will administer. Safe administration of BsAGs requires a stepwise approach.

Premedications for BsAGs

Premedications are a standard part of the administration protocol of any bispecific agent. Premedication is critical to reducing or mitigating AEs, including CRS. The timing and necessity of the premedication is important and may vary based on the specific agent, underlying disease, and phase of treatment. As a healthcare system prepares to utilize these agents, internal processes, protocols, and

order sets must be developed to ensure that the patient is receiving the appropriate premedication at the appropriate time.

Step-Up Dosing, Hospitalization, and Inpatient Versus Outpatient

Inpatient versus outpatient

Step-up titration-based dosing strategies are common when administering bispecific agents to reduce the risk of inflammatory side effects.[1,2] These strategies generally involve gradually increasing the dose of the BsAG therapy until the patient is at the therapeutic dose. The frequency, timing, and recommended site of care (inpatient or outpatient) of step-up dosing are agent-specific. Healthcare providers and organizations should refer to the agent's package insert for recommendations when developing administration processes.

Inflammatory side effects, including CRS, are common with BsAGs.[3] While hospitalization would allow for a more complete and closer management of AEs, there are several key aspects to consider, including the specific drug, the status of the patient, and local housing and proximity to the clinical site. While step-up dosing is commonly utilized to reduce the risk and severity of CRS, the logistics of mixing inpatient and outpatient administration and monitoring adds complexity to the treatment plan. The necessity of inpatient administration of BsAGs during step-up dosing will depend on the individual agent and the type of malignancy being treated (solid tumor vs hematological). Package inserts should be referenced when developing BsAG administration and step-up dosing protocols.

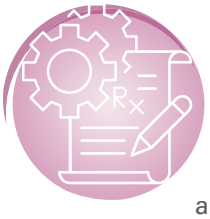
Both inpatient and outpatient administration and monitoring pose challenges. For patients admitted for step-up dosing, bed availability may be limited. Insurance authorization is required for treatment in either location, and is most often required for each hospital stay. Therefore, patients are often admitted and discharged at each dose, increasing the burden on the healthcare team and the patient. Treatment using this approach will require high levels of communication to seamlessly transition the patient from the outpatient to the inpatient setting. An excellent way of facilitating this transition can be through the engagement of nurse navigators or some other role dedicated to scheduling and coordinating treatment. This role may be responsible for coordinating both inpatient and outpatient labs as well as provider and infusion visits, all of which would be instrumental in reducing treatment delays. This role would also track community referrals, the number of patients on treatment, etc. This role is key for communication and making sure patients and providers feel supported.

The scope of services and hours of operation for outpatient management vary widely across practices. In general, to optimally manage BsAGs in the outpatient setting, practices should have the capacity to draw and process labs on-site, and must have adequate infusion space to allow for posttreatment monitoring. Both will allow practices to access the results necessary to guide treatment and facilitate AE management.

Patients treated with BsAGs may require extended monitoring and frequent visits, which places a large responsibility on the patient and caregiver. A key responsibility for both parties is arriving for each appointment on time to ensure the agent can be safely administered on the intended day of treatment. As mentioned, nurse navigators can be vital in helping the patient and caregiver manage these responsibilities and can ease the logistical burden on the patient.

Another key responsibility of the patient and caregiver is at-home AE recognition, management, and reporting. Due to the particularly insidious AE profile of bispecific agents, patient and caregiver

education on these 3 elements is critical to the successful management of disease at home. CRS and ICANS, which can be life-threatening, may be difficult for the caregiver to detect, particularly overnight. Subtle symptoms may be mistaken for something else and may delay reporting early CRS or ICANS to the healthcare team, placing the patient at increased risk. Patients may also present to the ED, where the staff does not have the full clinical picture and is attempting to treat an incorrect diagnosis.



Managing BsAG-Associated Adverse Events

Management of BsAG-associated AEs is a prime responsibility of the healthcare professionals administering the therapy. While the grade and incidence of AEs are agent-specific, most T-cell engaging bispecific agents carry a risk of CRS and ICANS.[3] Due to the potential severity of these events, it is important that the team is able to recognize early symptoms and deploy appropriate strategies to mitigate the risk of these AEs.

Cytokine Release Syndrome

CRS is a common and sometimes serious AE associated with BsAGs and other cellular therapies.[4] CRS is caused by a rapid release of cytokines from immune cells involved in immunotherapy.[4] The risk of CRS is greatest when first initiating therapy, but the specific time to onset is product-specific.[4] CRS can be difficult to recognize, as the hallmark symptoms are nonspecific. These characteristic symptoms include hypoxia, fever, and hypotension, which can also appear in a variety of other patient conditions, including but not limited to infection, dehydration, lung inflammation, pulmonary embolism, or pleural effusion.[3] CRS can also present with a variety of other symptoms based on the individual patient, including elevated liver enzymes, renal dysfunction, and neutropenia.[5] Therefore, a thorough differential diagnosis is necessary, involving appropriate labs, scans, and evaluation of comorbid conditions in order to implement appropriate treatment in a timely manner.

Ruling out other causes can be an onerous task but may involve the following clinical evaluations:

- A physical exam prior to administration of treatment and at regular intervals after treatment will also allow for early identification of CRS, ICANS, or other AEs
- Obtaining appropriate lab values and imaging scans:
  - Examples of general laboratory tests may include blood or sputum cultures, urinalysis, imaging (X-ray, computed tomography, etc)
  - Examples of CRS labs may include C-reactive protein, ferritin, complete blood count with differential, fibrinogen, and other labs as indicated for individual patients
- Evaluating comorbid/concomitant conditions: Is there another disease on the patient's profile that may be leading to these symptoms?

The oncology healthcare team is the best resource in executing CRS workup, as they have the highest level of understanding of the patient's baseline presentation, clinical picture, and any deviations from their baseline. The symptoms of CRS may be subtle, so comprehensive patient and caregiver education efforts regarding recognition of CRS symptoms, and how to contact the appropriate care team are crucial. In situations where patients need to present to the ED, it is recommended that the patient be evaluated at the healthcare system in which their oncology care team has practicing privileges. When this is not possible, an effort must be made to educate the treating ED staff on the patient's specific clinical picture and treatment plan. It is important that patients being treated with BsAGs carry a wallet

card with their name, diagnosis, treatment name, and start date, and the patient's oncology care team's contact information to be able to present to the ED staff. This will help streamline communication with the oncology care team to help the treating ED team guide the patient's workup.

CRS grading and treatment guidelines, such as those from ASTCT, should be readily accessible, as they can aid institutions in developing their own policies (Table 1). Other grading criteria such as CTCAE may be beneficial for institutions to reference when developing protocols.

Table 1. ASTCT CRS Grading Chart[3]

	Grade 1	Grade 2	Grade 3	Grade 4
Fever	≥38°C	≥38°C	≥38°C	≥38°C
WITH				
Hypotension	Absent	Not requiring vasopressors	Requires 1 vasopressor (with or without vasopressin)	Requires ≥2 vasopressors (excluding vasopressin)
AND/OR				
Hypoxia	Absent	Requiring low-flow nasal cannula or blow by (supplemental oxygen ≤6 L/min)	Requiring high-flow nasal cannula, facemask, non-rebreather mask, or Venturi mask for supplemental oxygen (≥6 L/min)	Requiring positive pressure (CPAP, BiPAP, intubation, and mechanical ventilation)

ASTCT, American Society for Transportation and Cellular Therapy; BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; CRS, cytokine release syndrome.

Management of CRS will depend on the grade and severity of the symptoms, emphasizing the need to establish a baseline and then determine the severity of any symptoms or clinical findings over the course of treatment. Since CRS can occur at varied phases of treatment, ongoing monitoring and grading are essential.

Patients experiencing grade 1-2 CRS may be treated symptomatically with supportive care. The supportive care interventions are dependent on the symptoms experienced and may include oxygen support, intravenous fluids, an antipyretic, an antihistamine, vasopressors, and perhaps a consideration for tocilizumab and glucocorticoid treatment.[6]

Patients experiencing grade 3-4 CRS require emergent care. If treated in the outpatient setting, patients will be hospitalized and will generally be transferred to the intensive care unit for close monitoring and intensive management.[6] Supportive care treatment may include similar treatments as in grade 1-2, such as intravenous fluids, an antipyretic, an antihistamine, and nausea treatment.[6] Pharmacological treatment will include tocilizumab and dexamethasone.[6]

Table 2 shows a sample CRS treatment program adapted from BC Cancer Center, although individual recommendations on product-specific CRS management should be obtained from the manufacturer.

Aside from drug therapy, there can be other aspects that ensure success in the management of CRS. Institutions with telemetry and virtual observation technologies are encouraged to utilize these for patient care. Designing optimal workflows and checklists that aid the healthcare team in ruling out other causes

Table 2. Sample CRS Management Recommendations[6]

CRS grade	Administer
1	• Symptomatic management and monitoring. Symptomatic management may include: ◦ Consider IV fluids ◦ Acetaminophen 650 or 975 mg PO every 4 hours as needed ◦ Diphenhydramine 50 mg IV every 4 hours as needed ◦ Metoclopramide 10 mg PO/IV every 4 hours as needed ◦ Ondansetron 8 mg PO/IV every 8 hours as needed
2	• Utilize same PRN drugs as in grade 1 for symptomatic management • Depending on cancer type, administer tocilizumab or steroids. Generally, tocilizumab will come first, except in melanoma patients, who are more responsive to steroids • Tocilizumab 8 mg/kg, max 800 mg/dose (limit 3 doses in a 24-hour period) • Dexamethasone 10 mg IV every 6 hours OR methylprednisolone 1 mg/kg IV every 12 hours Continue until CRS is less than grade 1, then taper over 3 days
3 and 4	• Admit to intensive care unit for management • Utilize same PRN drugs as in grade 1 for symptomatic management • Tocilizumab 8 mg/kg, max 800 mg per dose every 8 hours • Dexamethasone 10 mg IV every 6 hours OR methylprednisolone 1 g IV every day for 3 days Continue corticosteroids until CRS is grade 1 or less, then taper over 3 days

CRS, cytokine release syndrome.

of CRS symptoms can ensure consistency and accuracy in patient evaluation. Finally, developing institution-specific CRS management guidelines based on severity that explicitly outline what criteria to look for, what supportive care to give, and when to transfer to a higher level of care, is recommended.

Immune Effector Cell-Associated Neurotoxicity Syndrome

ICANS is a serious side effect that a patient may experience while on immune therapy. ICANS is largely manageable and can be characterized by aphasia, tremors, dysgraphia, and lethargy.[3] Like CRS, ASTCT has published a grading criterion for ICANS that may be helpful to institutions when developing their own protocol (Table 3).

The symptoms of ICANS are patient-specific (handwriting, recall, motor function) and require consistency in assessment both by the healthcare team and by the caregiver. A core part of grading ICANS involves evaluating the patient's ICE score, which is an objective scoring tool used in grading neurologic domains of speech, orientation, attention, language, and handwriting (Table 4). It is recommended that a baseline ICE score be obtained prior to starting a patient on BsAGs.

Aside from obtaining the baseline ICE score and performing a neurological exam on the patient for ICANS grading, there are several considerations recommended in the continuous management of the patient. For example, training team members how to scan and access the patient's samples in a consistent location within the EHR can be crucial for evaluating the presence of ICANS in both the inpatient and outpatient setting. This can be done in a specialized media tab, a flowsheet, or can be as simple as snipping the printed completed tool into the nurse's clinical documentation. This needs to be a consistent practice across the institution to standardize nurses' clinical evaluations across the healthcare system.

Table 3. ICANS Grading Criteria[3]

Neurotoxicity domain	Grade 1	Grade 2	Grade 3	Grade 4
Immune effector cell-associated encephalopathy (ICE) score	7-9	3-6	0-2	Patient is unarousable or unable to assess
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous tactile stimuli. Coma or stupor
Seizure	N/A	N/A	Any clinical seizure (focal or generalized) that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (>5 min) or repetitive clinical or electrical seizure without return to baseline in between
Motor findings	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis
Elevated intracranial pressure				
Cerebral edema	N/A	N/A		Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve V1 palsy, papilledema, or Cushing's triad

EEG, electroencephalogram; ICANS, immune effector cell-associated neurotoxicity syndrome; N/A, not applicable.

Table 4. ICE Scoring Criteria[3]

Immune effector cell-associated encephalopathy (ICE) score		
Orientation	Orientation to year, month, city, and hospital	4 points
Naming	Ability to name 3 objects (eg, point to items like clock, pen, button)	3 points
Following commands	Ability to follow simple commands (eg, “show me 2 fingers”)	1 point
Writing	Ability to write a standard sentence (eg, “an apple is a fruit”)	1 point
Attention	Ability to count backwards from 100 by 10	1 point

Grade 1-2 ICANS may require treatment to be held, supportive care of seizure prophylaxis with levetiracetam, and a consideration for glucocorticoid treatment.[5] More severe grades or resistant ICANS will require scheduled glucocorticoid treatment, supportive seizure care with benzodiazepines or anticonvulsants, and a transfer to the intensive care unit.[5] Brain imaging and a consult to neurology are recommended to evaluate for other underlying processes.[5]

Monitoring Protocols for BsAGs

As with all immunologic therapies, having proper and routine monitoring is crucial to assessing the progress of the patient and identifying potential complications early. Consistent monitoring guided by evidence-based protocols is recommended for healthcare centers looking to initiate BsAG therapy.

Development of Monitoring Protocol

Development of monitoring protocols can take many forms and can involve a variety of staff. A focus group of nurses cited that developing these protocols requires input from a multidisciplinary team, including clinical operations, pharmacists, physicians, quality managers, and more. As discussed previously, developing protocols, workflows, and resources to support administration of bispecific agents has numerous considerations past the clinical aspect, and requires coordination from a variety of team members. Engaging all stakeholders in the process will build a team that is well-versed in the overall elements of the program. This team can champion both the overall process and their individual roles and is likely to develop resources that correctly reflect that role. Having several differing perspectives on the protocol development team can aid in creating a comprehensive and user-friendly monitoring process for all care team members.

Postdose Monitoring

Regular outpatient monitoring is essential following initial inpatient dosing. This involves educating patients and caregivers on how and how often to conduct assessments, ensuring they have the appropriate tools to do so, what symptoms to report, and contact procedures. When developing monitoring protocols, it is imperative to understand the individual challenges between inpatient and outpatient settings to develop processes that uniquely resolve these challenges, setting the patient up for success.

Patient and Caregiver Preparation and Expectations

After the initial infusion and monitoring period, the monitoring responsibility will shift from the healthcare provider to the patient and caregiver. Thus, it is crucial that ample and effective education is provided to both the patient and/or caregiver to effectively monitor for side effects of BsAGs.

Patient Education

Patient education should be an ongoing process, starting before the patient receives their treatment and continuing throughout their cancer journey. Each phase of treatment may look slightly different from the educational perspective but should always be tailored to maximize patient and caregiver understanding.

Before initiation of treatment, patient education will focus more on the agent being received, the specifics of administration, and the logistics required for treatment. This can include but is not limited to agent overview, AE profile, premedication, step-up dosing, possible dose delays, and logistics of initial hospitalization. Patients need to be educated on the requirements for bispecific therapy, such as the need to be in close proximity to their treating healthcare center or an ED during the initial infusion phase, any lodging needs, and procedures for when emergency care is needed.

The goal should be to make the patient comfortable in understanding their treatment, including the goals of treatment, how it will be administered, and potential side effects. These aspects may also be discussed during the administration or initial hospitalization for bispecific treatment, with a focus on addressing the patient's specific concerns.

After the initial administration and monitoring, patient education will emphasize several key points. During discharge, a protocol for transitioning to the outpatient setting should be delivered both verbally and in writing by skilled nursing staff. Critical portions of a discharge protocol may include the following:

1. Reviewing expectations for monitoring and assessing AEs to be performed by the patient and caregiver, with a teach-back approach to ensure comprehension. Both the patient and the caregiver should demonstrate understanding of the most serious AEs, how to recognize them, how to monitor them effectively, and which AEs require emergent reporting
2. Reviewing CRS and ICANS symptoms, as these signs may be vague and not reported by the patient or caregiver
3. Providing details on logistics, such as the patient's care team, how to contact them, and the schedule for follow-up visits, is integral to the patient's success

Patient education on selected AEs should include the following, as well as be individualized to the patient's bispecific therapy:

- CRS: Understanding the hallmark symptoms of CRS, emphasizing the nonspecific nature of these symptoms, keeping a thermometer in the house, developing a temperature check schedule, keeping a log of temperatures to bring to appointments, emergent versus nonemergent temperature, utilizing pulse oximeter to check oxygen levels
- ICANS: Having an identified caregiver physically available to monitor for subtle neurological changes, understanding the hallmark symptoms of ICANS, seizure management, obtaining handwriting samples, bringing samples to appointments, and basic, patient-friendly ICE assessment
- Other AEs: Management strategies for xerostomia, rash, taste disturbances, dry skin, dysphagia, or other patient-specific symptoms

Patients should be provided with the specific procedures for how to detect AEs that require immediate notification of the care team, and how and whom to contact within the team to allow the team to provide guidance on management before reporting to the ED. Patients should be provided with a direct line to clinical support staff to reduce the time and burden as well as to encourage patient engagement. If the center allows it and it is warranted, same-day appointments with a space ready to manage the patient would be ideal.

If patients are unable to access their specific care team, it is acceptable to utilize emergency services. However, every effort should be made on the part of the patient to relay their specific condition and treatment to emergency services staff to ensure optimal management. A wallet card as described earlier can be an optimal way to communicate this information to ED staff.

Caregivers are recommended for all patients receiving BsAGs. Caregiver requirements should be included in the institutional protocol for BsAGs administration and follow-up. If a patient who does not have a caregiver desires one or the team believe that they need one, engaging with the institution's social worker, discharger planner, or case manager to arrange for a caregiver will be a necessary step in their care plan.

Caregivers may be family members or healthcare professionals that assist the patient in their home daily or at regular intervals. The needs the caregivers may be tending to will depend on the individual

patient; some patients may need regular care from home health aides; others may need more intensive care at a skilled nursing facility. Based on the individual patient's needs, the care team may perform an insurance benefits investigation to ensure the patient can receive the optimal level of care at a non-prohibitive cost. Afterwards, a discussion with the patient will guide what level of care will be provided. Caregiver services provided to the patient may be acquired through the following:

- Organization's own home health or skilled nursing division
- Working with the state's Department of Aging
- Through private caregiver organizations

All identified caregivers should receive the same level of education as the patient. This will include all the points already discussed, and may include additional information such as setting up adequate transportation needs (if the patient is unable to drive) to accommodate the patient's treatment schedule.

Emphasis should be placed on caregiver availability. A caregiver should be available to the patient 24/7, and according to the nurses' panel, this should be someone whom the patient can always see and touch. Even when the patient is getting their treatment and under the care of skilled staff, the caregiver should make every effort to stay with the patient.

Conclusion

BsAGs, while being a new and exciting treatment option for those with solid tumors, do require organizational preparation to safely, effectively, and efficiently provide therapy to patients. Operational elements like identifying the optimal champions to lead BsAG implementation efforts, creating tailored learnings for healthcare staff, and standardizing organization procedures are keys to success. Furthermore, a strong clinical understanding by medical staff of the possible adverse events and how to both prevent and manage them ensures patients will receive the best possible experience at your organization. Utilizing the operational and clinical principles discussed in this resource guide as well as individualizing them to your unique practice can help ensure the successful implementation and continued ease of management of a BsAG program for solid tumors.

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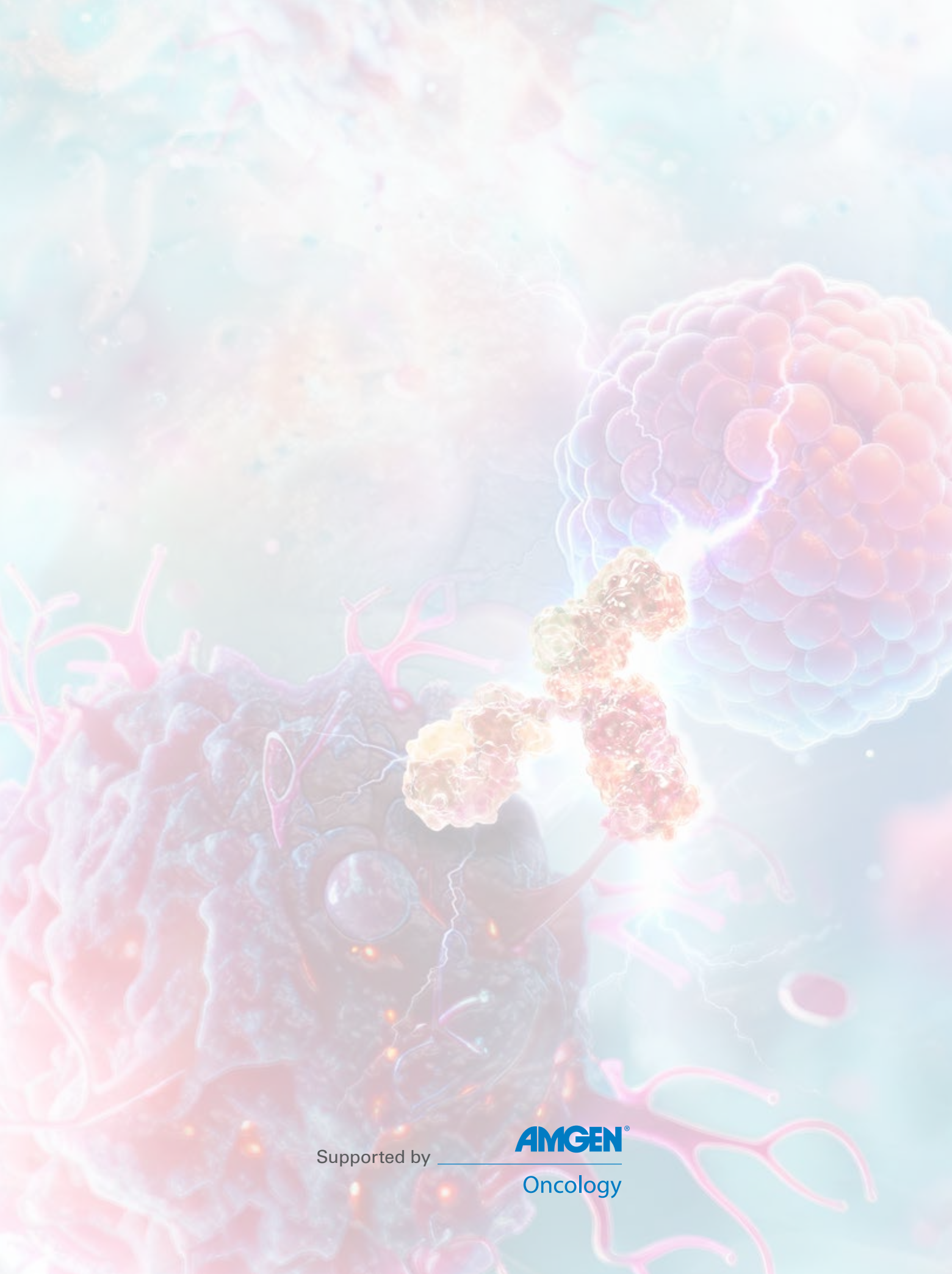

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