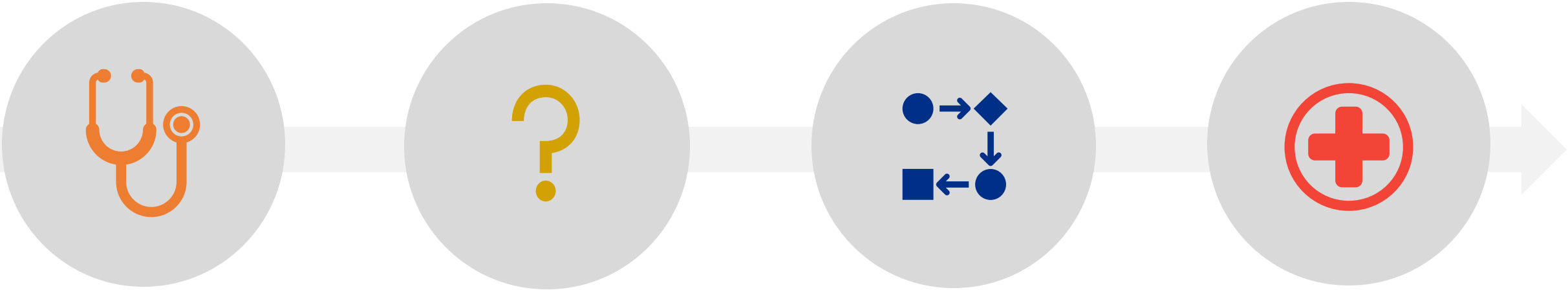
Integrating New Treatments into Practice:
Panel Discussion on Bispecific Antibodies in the Community Setting

Cornerstone National Conference

Dallas, TX

March 15, 2025

Why are we doing this?



BISPECIFICS REPRESENT A NEW MILESTONE IN THE TREATMENT OF PATIENTS

INTEGRATION INTO COMMUNITY ONCOLOGY PRESENTS CHALLENGES

ALIGNING ON ACTIONABLE STEPS TO MAKE THIS A VIABLE OPTION LEADS TO VALUE FOR PRACTICES

AND ULTIMATELY IMPROVES TREATMENT AND MANAGEMENT OF PATIENTS FOR BETTER PATIENT OUTCOMES

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Panel Discussion on Bispecific Antibodies in the Community Setting

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Georgia Cancer Specialists

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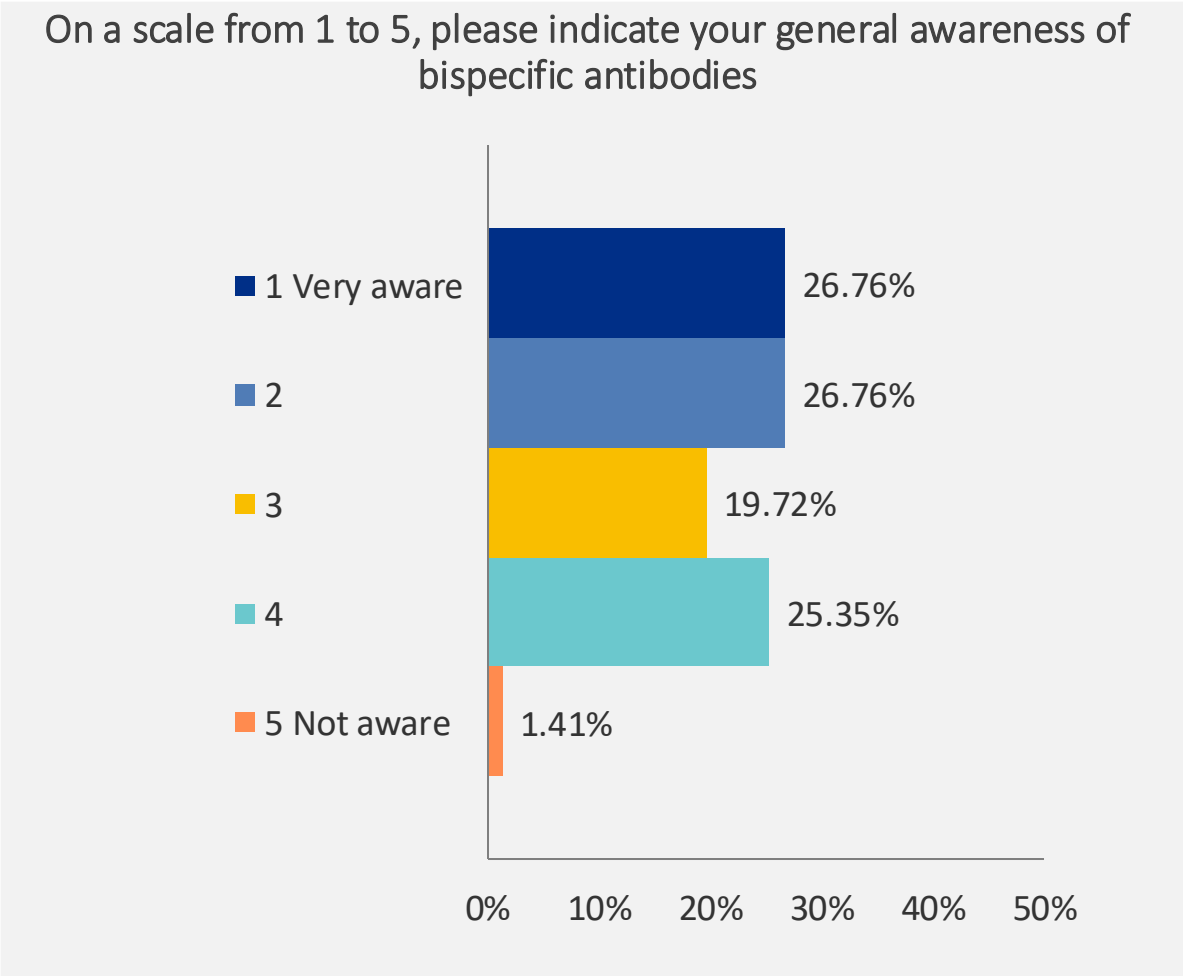
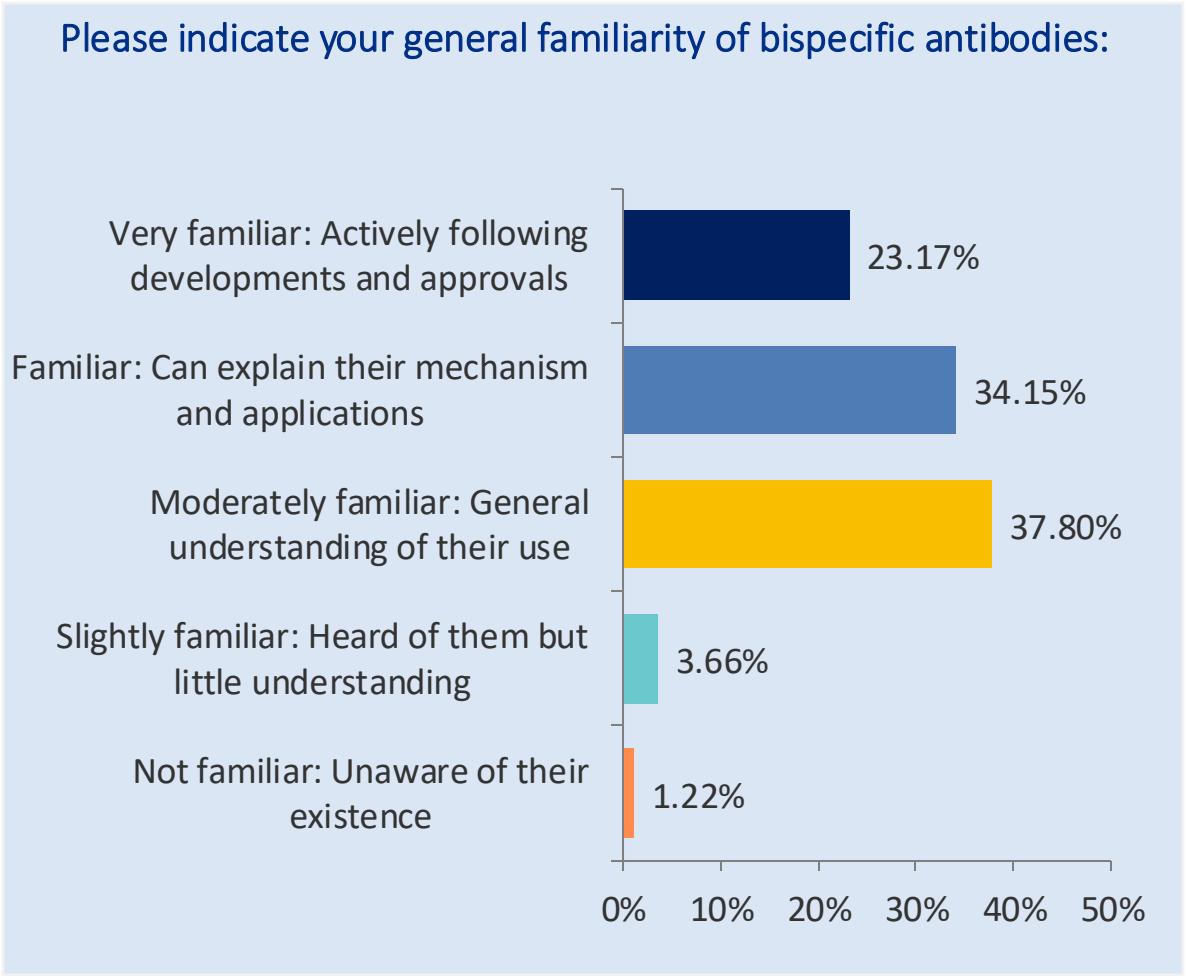
Highlands Oncology Group

February 2024 Survey



Answered: 71

December 2024 Survey



Answered: 81

Why are we doing this?

BISPECIFICS REPRESENT A NEW MILESTONE IN THE TREATMENT OF PATIENTS

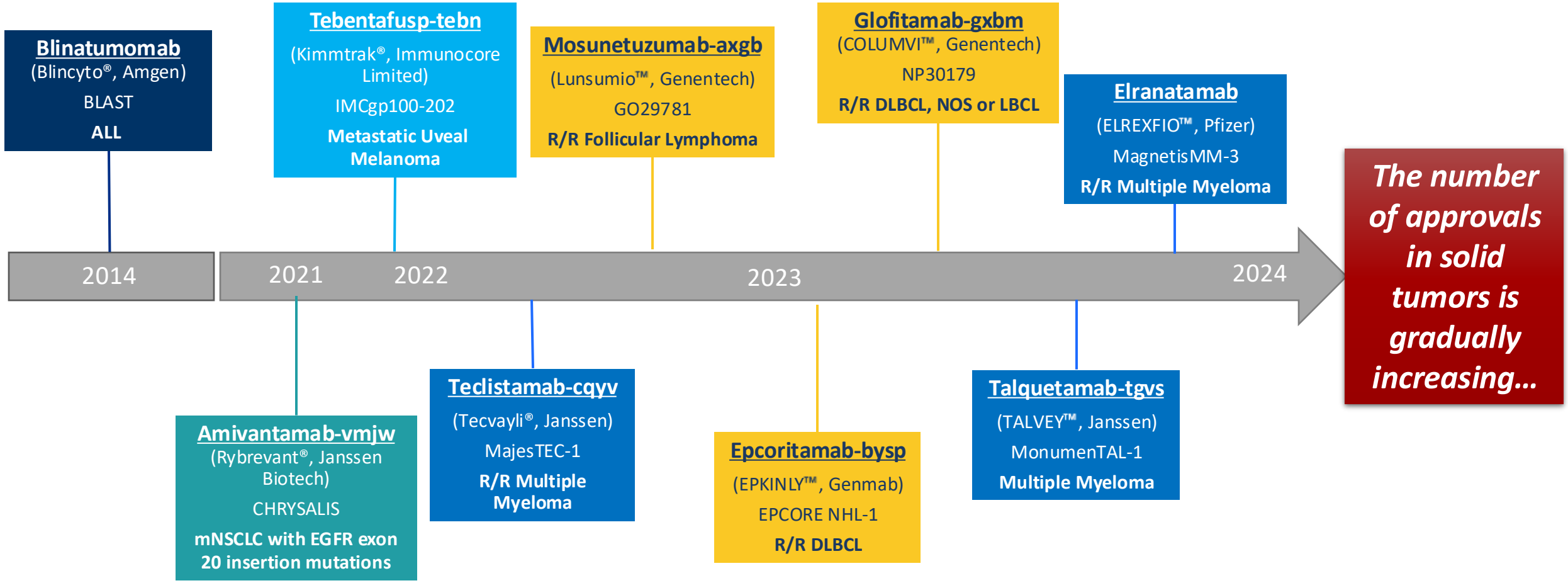
INTEGRATION INTO COMMUNITY ONCOLOGY *STILL* PRESENTS CHALLENGES

ALIGNING ON ACTIONABLE STEPS TO MAKE THIS A VIABLE OPTION LEADS TO VALUE FOR PRACTICES

AND ULTIMATELY IMPROVES TREATMENT AND MANAGEMENT OF PATIENTS FOR BETTER PATIENT OUTCOMES

Las Vegas April 2024

Bispecifics: Developmental Timeline in Oncology



FDA Approvals of New Bispecific Therapies, 2024

Approval Date	Name	Manufacturer	Targets	Indication
May 16, 2024	**Tarlatamab (Imdelltra)**	**Amgen**	**DLL3 and CD3**	**Previously treated extensive stage small cell lung cancer**
June 14, 2024	Blinatumomab (Blincyto)	Amgen	CD19 and CD3	Consolidation in CD19-positive Philadelphia chromosome-negative acute lymphoblastic leukemia
June 26, 2024	Epcoritamab (Epkinly)	Genmab/AbbVie	CD20 and CD3	Relapsed/refractory follicular lymphoma

Key Question

What are the benefits of implementing bispecific therapy programs in the community setting?

Frequent dosing, distance to academic / hospital, time away from home, and requirement for a caregiver companion are too burdensome for some patients and often forego treatment

Bispecific antibodies delivered in an outpatient setting increases access to advanced therapies in community settings and reduces the burden of travel for patients

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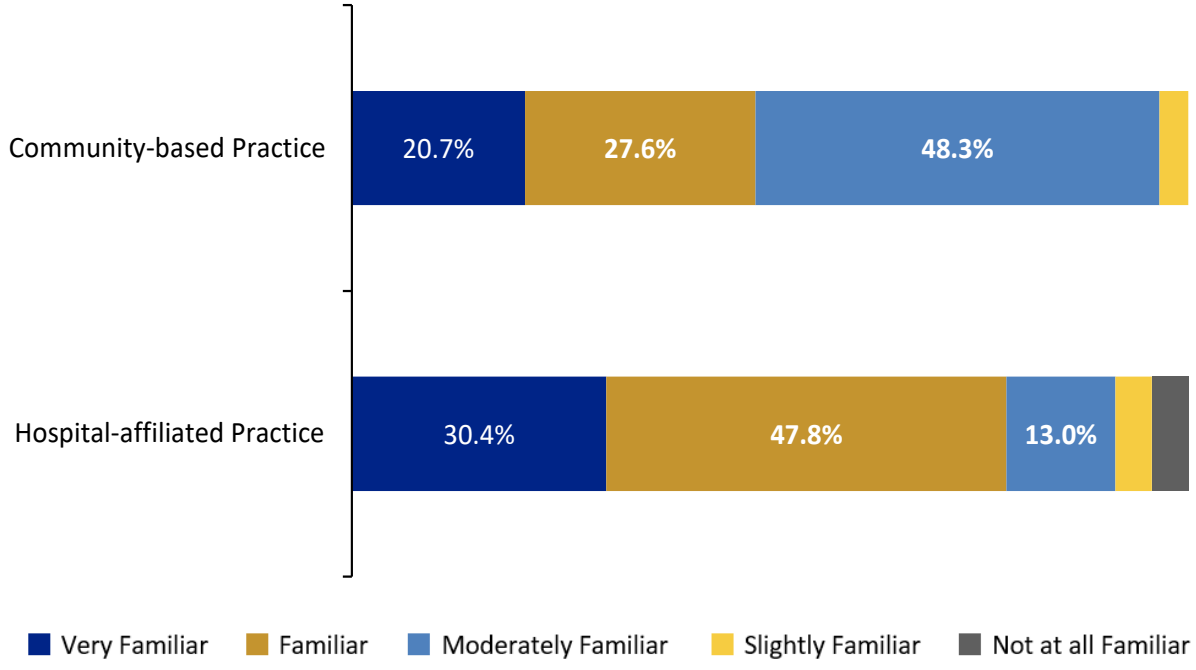
December 2024 Survey

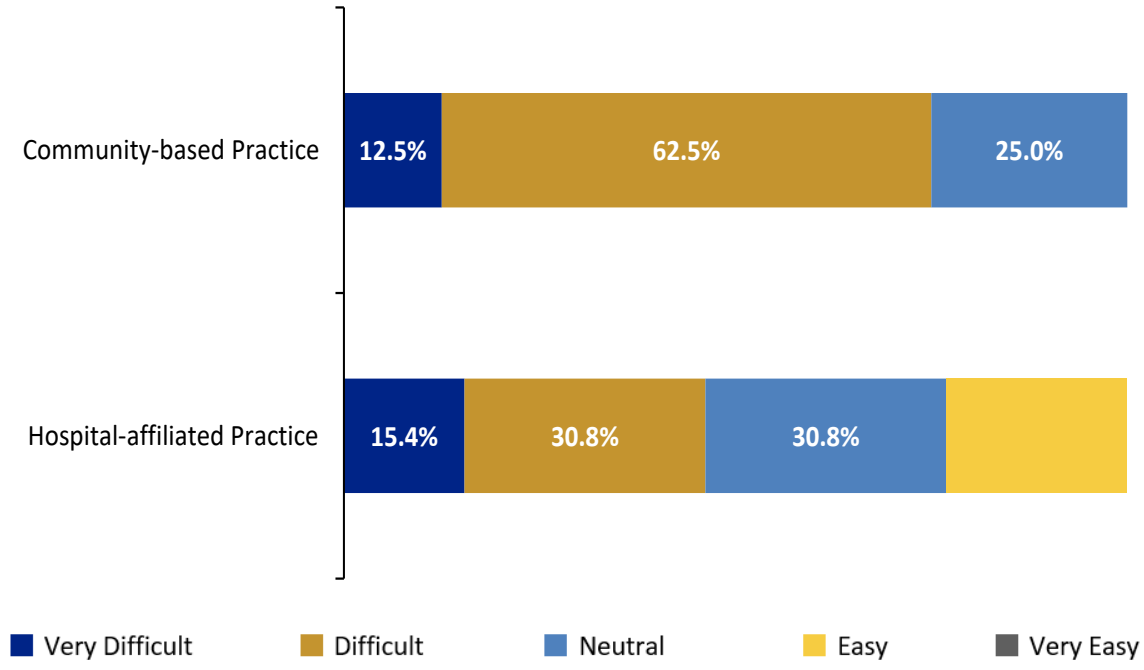
Across both Community-based (CB) and Hospital-affiliated (HA) practices familiarity of bispecific antibody therapies is strong

Please indicate your general familiarity of bispecific antibodies:



In both Community-based practices and the Hospital-affiliated practices, bispecific antibodies are considered difficult to integrate into practice

How would you rate the ease of integrating bispecific antibody therapies into your practice?



Answered: 58 CB; 23 HA

Key Question

What factors might influence the decision to administer bispecifics in a community setting instead of at an academic center?

Access and experience or comfort with administration and monitoring and managing toxicities in a community setting

Disease type (DLBCL versus less aggressive), comorbidities, place in treatment journey (3L patients can be very different from 2L)

Data to support use in earlier lines of therapy for more “healthy” patients

Patient selection and co-management with academic/hospital, with clear communication and expectations

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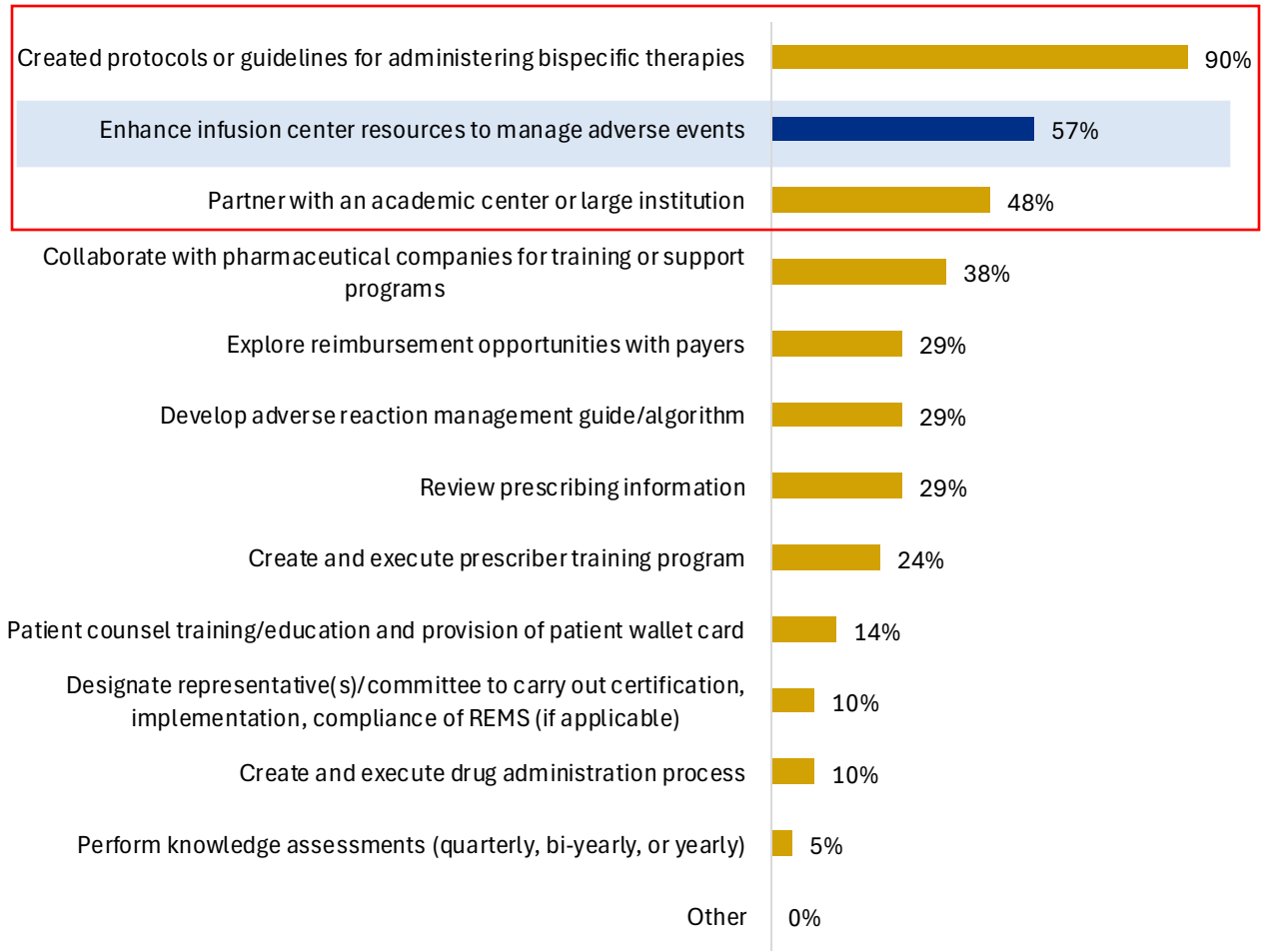
December 2024 Survey

Top three steps towards incorporating bispecific antibodies into practice: *Creating protocols, partnering with an academic center, and enhancing infusion center resources to manage adverse events*

Community-Based Practices *(n: 45)*

Hospital-Affiliated Practices *(n: 21)*



Key Question

What steps do you take to enhance infusion center resources to manage adverse events associated with bispecifics?

Consider step up dosing and needs related to T-cell toxicities associated with T-cell engagers

Consider the target of the bispecific and identify the related toxicities…prepare accordingly

e.g., **talquetamab-tgvs**, which targets a protein that is also present in keratin-expressing hair follicles and cells in the oral cavity; can lead to oral toxicities such as taste changes that may be permanent, dry mouth, and dysphagia, as well as skin toxicities.

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Case-based Discussion for Integration of Bispecific Antibodies into Practice

Panel Discussion on Bispecific Antibodies in the Community Setting

1. *Financials and logistics*
2. *Toxicity management*
3. *Transitioning patients*

Real World Patient Case #1: IgG kappa Multiple Myeloma

63 yr-old male diagnosed with IgG kappa MM May 2020

- Initial bone marrow
  - Monoclonal plasmacytosis of 80-90% with step-up cytogenetics by FISH (*CCND1*/IgG rearrangement)
    - Monosomy 13 / del(13q)
    - Monosomy 17 / del(17p)
    - Loss of B Cell Receptors (BCMA)
    - Normal male karyotype

1st Line Therapy

- **Carfilzomib, lenalidomide, and dexamethasone (KRd)**
  → Tandem autologous SCT
  November 2020 to May 2021
- **Daratumumab + lenalidomide July 2021 post transplant maintenance**
  → December 2021 stopped lenalidomide

Bone marrow biopsy was completed December 5th, 2023 for evaluation of leukocytosis. Pathology showed marrow plasmacytosis accounting for 90% of marrow cellularity

2nd Line Therapy

- **Initiated teclistamab**
  → January 2024

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Real World Patient Case #1: IgG kappa Multiple Myeloma

63 yr-old male diagnosed with IgG kappa MM May 2020

1st Line Therapy

- **Carfilzomib, lenalidomide, and dexamethasone (KRD)**

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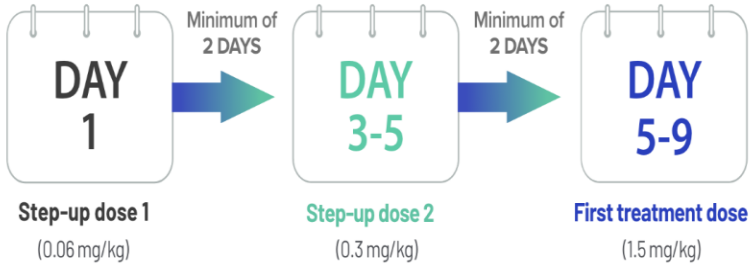
2nd Line Therapy

- **Initiated teclistamab January 2024**

Step-up Dosing



Prior to starting treatment with TECVAYLI®

- Consider initiation of antiviral prophylaxis to prevent herpes zoster reactivation

1 to 3 hours before step up dose to reduce risk of CRS

- Corticosteroid, Histamine-1 (H1) receptor antagonist, Antipyretics

Dosing & Administration | TECVAYLI® (teclistamab-cqyv) HCP

- ***Location of step-up dosing***
- ***Logistics of transitioning patients***
- ***Consistency of Protocols across institutions***
- ***Financial logistics***

Real World Patient Case #1: IgG kappa Multiple Myeloma

63-yr-old male diagnosed with IgG kappa MM May 2020

1st Line Therapy

- **Carfilzomib, lenalidomide, and dexamethasone (KRD)**

  → Tandem autologous SCT November 2020 to May 2021

- **Daratumumab + lenalidomide July 2021 post transplant maintenance**

  → December 2021 stopped lenalidomide

2nd Line Therapy

- **Initiated teclistamab January 2024**

CRS/ICANS are mainly acute reactions that occur during step-up dosing…

But what about the risk of adverse events that can increase with subsequent treatments and continue with long term treatments?

Adverse event management

→ **Recurrent infections on teclistimab**

- Recurrent pneumonias (three episodes) July 2024 to November 2024 with atypical organisms
- Initiated on IVIG to goal IgG >600
- Resolution of infections

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Cytokine Release Syndrome (CRS)

BsAbs have a relatively short half-life (compared to CAR T-cell therapy) and need to be administered repeatedly, therefore CRS symptoms tend to resolve relatively quickly by interrupting therapy and providing supportive care

- *Educate staff and develop toxicity management protocols*
- *Ensure tocilizumab is available*
- *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*
- *Remind patients and their caregivers about signs and symptoms of CRS*

ASTCT CRS Consensus Grading

CRS Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever	Temperature ≥ 38°C	Temperature ≥ 38°C	Temperature ≥ 38°C	Temperature ≥ 38°C
			With	
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
			And/or	
Hypoxia	None	Requiring low-flow nasal cannulaz or blow-by	Requiring high-flow nasal can nulaz, facemask, nonrebreather mask, or Venturi mask	Requiring positive pressure (e.g., CPAP, BiPAP, intubation and mechanical ventilation)

Premedication reduces CRS rates

Steroids

Tocilizumab

Organ toxicities associated with CRS may be graded according to CTCAE v5.0 but they do not influence CRS grading.

D.W.Lee et al./BiolBloodMarrowTransplant 25 (2019): 625-638

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Immune effector cell-associated neurotoxicity syndrome (ICANS)

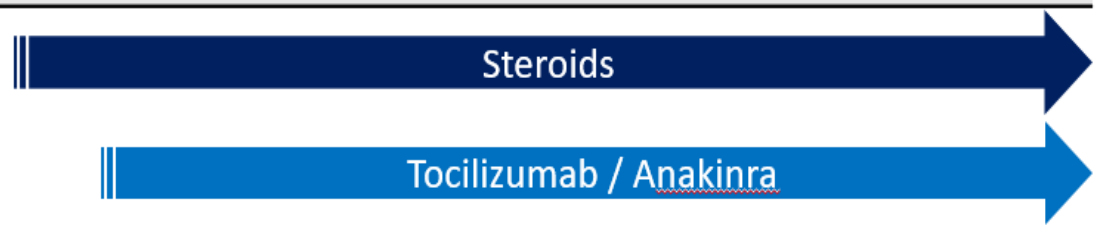
ICANS can manifest with a range of effects, from mild symptoms like headaches to more severe conditions such as confusion, unconsciousness, and seizures

- *Early intervention is critical to be able to give the next dose*
- *Collaboration of neurologist and neuroradiologist is important*
- *Increase the dose (dexamethasone, anakinra) if not responding*
- *Avoid concurrent medications that might cause cognitive changes*

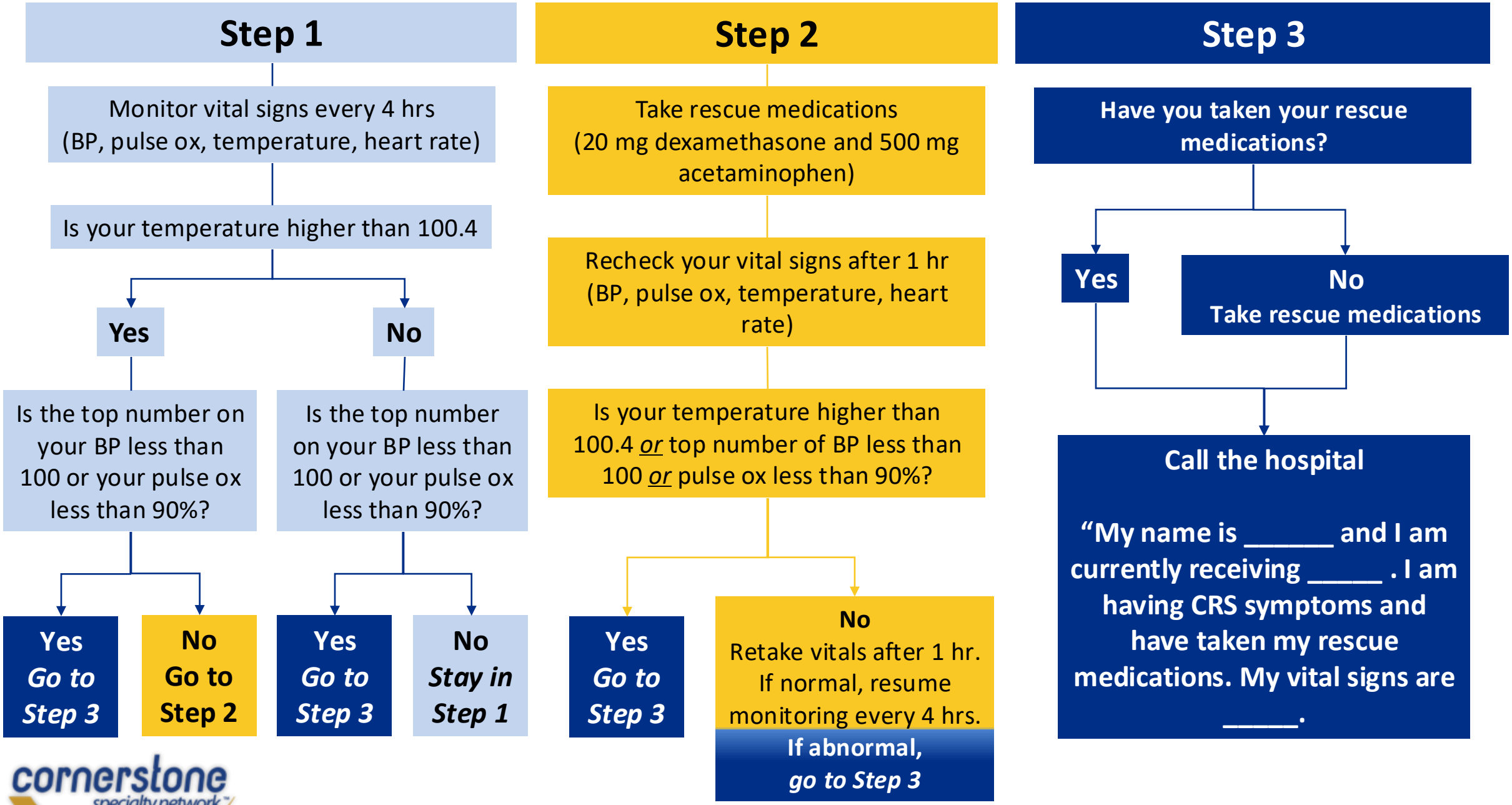
ASTCT ICANS Consensus Grading

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score	7-9	3-6	0-2	0 (patient is unarousable and unable to perform ICE)
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse. Stupor or coma
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 seizures without return to baseline in between
Motor findings	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
Elevated ICP/ cerebral edema	N/A	N/A	Focal/local edema on neuroimaging	Diffuse cerebral edema on neuroimaging; decerbrate or decorticate posturing; or cranial nerve VI palsy; or papilledema; or Cushing's triad

ICANS grade is determined by the most severe event



Consensus Recommendations on the Management of Toxicity Associated with CD3xCD20 Bispecific Antibody Therapy
Blood. 2024 Jan 22:blood.2023022432. doi: 10.1182/blood.2023022432. Online ahead of print.



Real World Patient Case #2: IgG kappa Multiple Myeloma

61-year-old male diagnosed with MM October 2020

- MRI thoracolumbar spine showed numerous lesions
- Labs showed kappa 22.4, lambda 60.0, ratio 0.37; IgG 4273; IFE with IgG lambda and SPEP with M spike 2.7g; beta 2 microglobulin 2.55, LDH 106.9.
- Bone marrow biopsy showed hypercellular marrow (70%), with 80-90% plasma cells with 44% plasma cells showing monoclonality; FISH with trisomy 9, deletion 13q, loss of 5'IGH, loss of MAF; normal male karyotype

1st Line Therapy

- **Bortezomib, lenalidomide, dexamethasone (RVd)**
  - → Consolidation with autologous SCT June 2021
  - → Maintenance lenalidomide September 2021

Disease relapse March 2022 (#1)

2nd Line Therapy

- **Daratumumab, carfilzomib, and dexamethasone (DKd)**

Disease relapse July 2022 (#2)

3rd Line Therapy

- Cytoreduced with cyclophosphamide as bridge to **CAR T trial** (Novartis PHE885)
  - → Received CAR T November 2022
  - Course was complicated by Grade 1 CRS (persistent fevers); he received tocilizumab x2 and dexamethasone x1

Disease relapse July 2023 (#3)

4th Line Therapy

- **Car T: ciltacabtagene autoleucel** (Carvykti)
  - → Received CAR T September 2023

Disease relapse (#4)

5th Line Therapy

- **Talquetamab**
  - **April 2024 - October 2024**

Step-up Dosing with Q2W and QW dosing available, SQ

1 to 3 hours before each step-up dose

- *Corticosteroid, Antihistamines. Antipyretics*

Dosing | TALVEY® (talquetamab-tgvs) HCP

Real World Patient Case #2: IgG kappa Multiple Myeloma

1st Line Therapy

- **Bortezomib, lenalidomide, dexamethasone (RVd)**
  → Consolidation with autologous SCT
  June 2021 Maintenance lenalidomide
  September 2021

Disease relapse March 2022 (#1)

2nd Line Therapy

- **Daratumumab, carfilzomib, and dexamethasone (DKd)**

Disease relapse July 2022 (#2)

3rd Line Therapy

- **CAR T trial (Novartis PHE885) November 2022**
  - Course was complicated by Grade 1 CRS (persistent fevers); he received tocilizumab x2 and dexamethasone x1

Disease relapse July 2023 (#3)

4th Line Therapy

- **CAR T: ciltacabtagene autoleucel (Carvykti)**
  → September 2023

Disease relapse (#4)

5th line Therapy

- **Talquetamab April 2024 - October 2024**

Adverse event management

→ **Skin Toxicity**

- Grade II/III skin toxicity
- Treated with barrier creams, moisturizers, antihistamines, and topical --> systemic steroid; used nail hardeners, topical vitamin E, antibiotic ointments, and nail trimming
- Skin toxicity labeled as psoriasis by dermatology but did not account for nail changes

Disease relapse (#5)

- Improvement in skin, nail condition within 2 months of discontinuation
- Treated with cyclophosphamide as bridge to salvage autologous SCT

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Real World Patient Case #3: Triple HIT DLCBCL

53-year-old male diagnosed with Triple HIT DLCBCL in 04/2024

1st Line Therapy

- **DA-RE-EPOCH**
  - ➢ **Consolidative CAR-T (at MDA) on 7/17/2024**

Progressive disease on imaging 01/2025

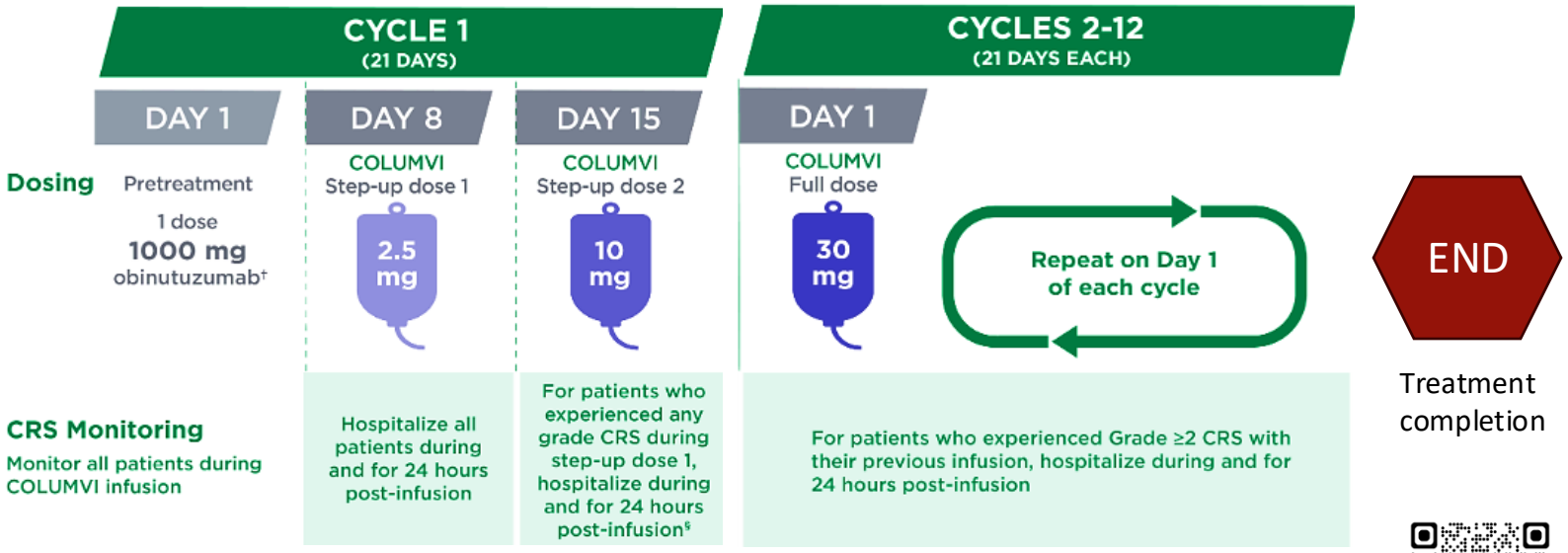
2nd Line Therapy

- **Glofitamab/Gem/Ox**

Adverse event management

- Grade 2 CRS in office
  - Toci

Step-up Dosing



COLUMVI™ (glofitamab-gxbm) dosing schedule | HCP

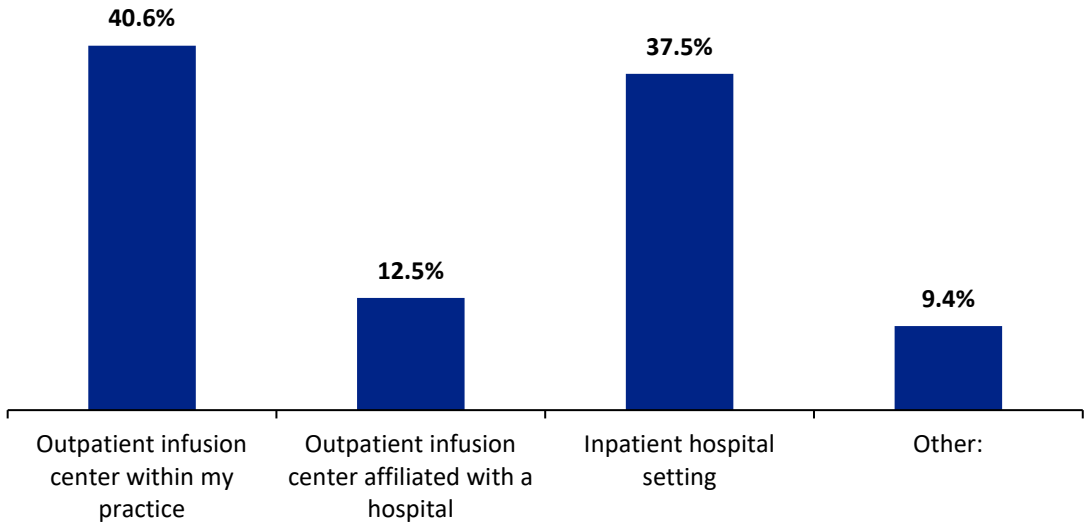
December 2024 Survey

41% of Community-based respondents indicated that step-up dosing takes place at an *Outpatient Infusion Center within their practice*.

54% of Hospital-affiliated respondents indicated that step-up dosing takes place in an *Inpatient Hospital Setting*.

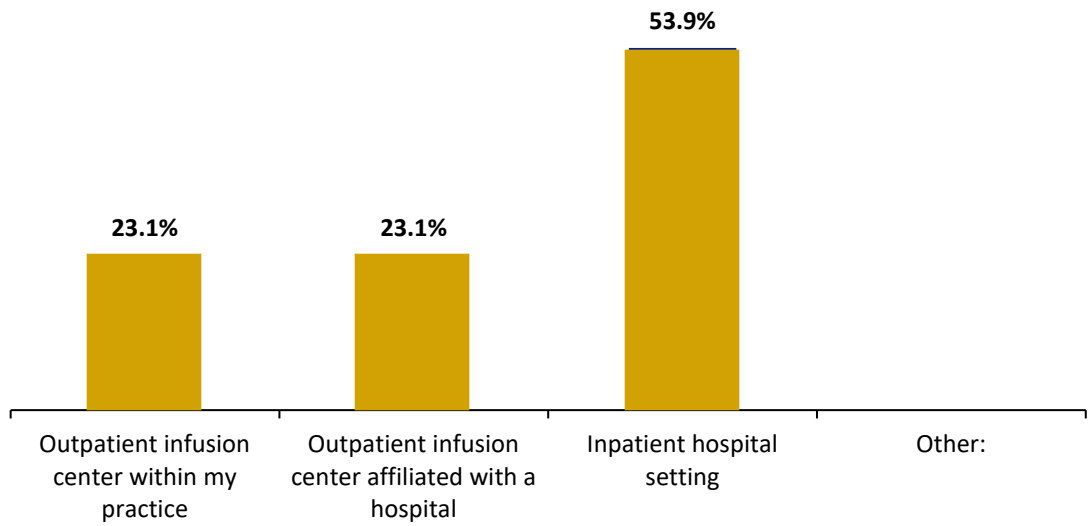
Community-Based Practices *(n: 32)*

In what setting does the step-up dosing take place for bispecific antibody therapies?



Hospital-Affiliated Practices *(n: 13)*

In what setting does the step-up dosing take place for bispecific antibody therapies?



Key Data

DeLLphi-300

To report safety outcomes in patients treated with tarlatamab 10 mg IV Q2W followed by either 6–8-hour outpatient or 48-hour inpatient monitoring in cycle 1 in the phase 1 DeLLphi-300 study (*Presented at ESMO Immuno-Oncology Congress 2024 Poster 115P*)

Study Design:

- Non-randomized comparative analysis
  - Age ≥ 18 years • SCLC that progressed or recurred following ≥ 1 platinum-based regimen • ECOG PS 0–2 • Stable, treated brain metastases allowed
- Patients treated with tarlatamab
  - **Cycle 1:** Day 1, 1 mg → Day 8, 10mg → Day 15, 10 mg
  - **Cycle 2+:** 10 mg IV Q2W

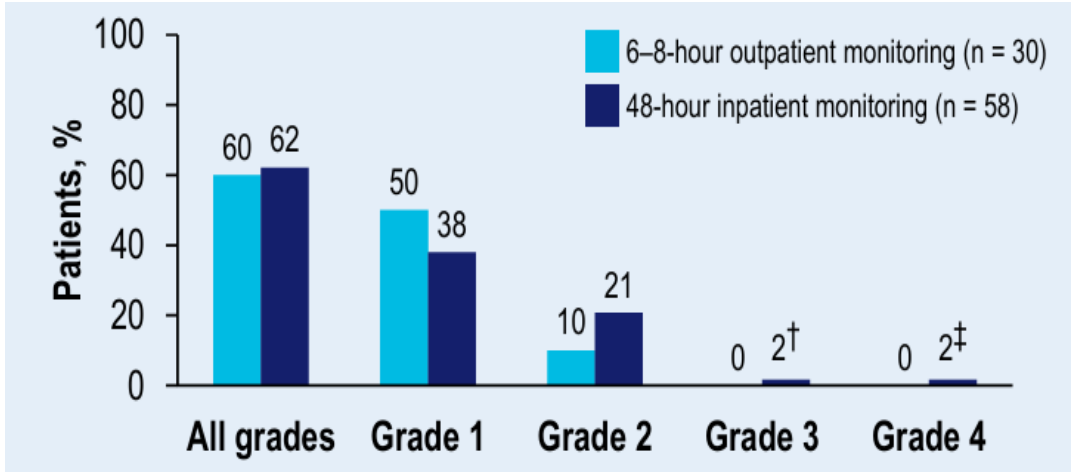
Monitored for ***6–8 hours in the outpatient**** setting in cycle 1 (n=30)

vs

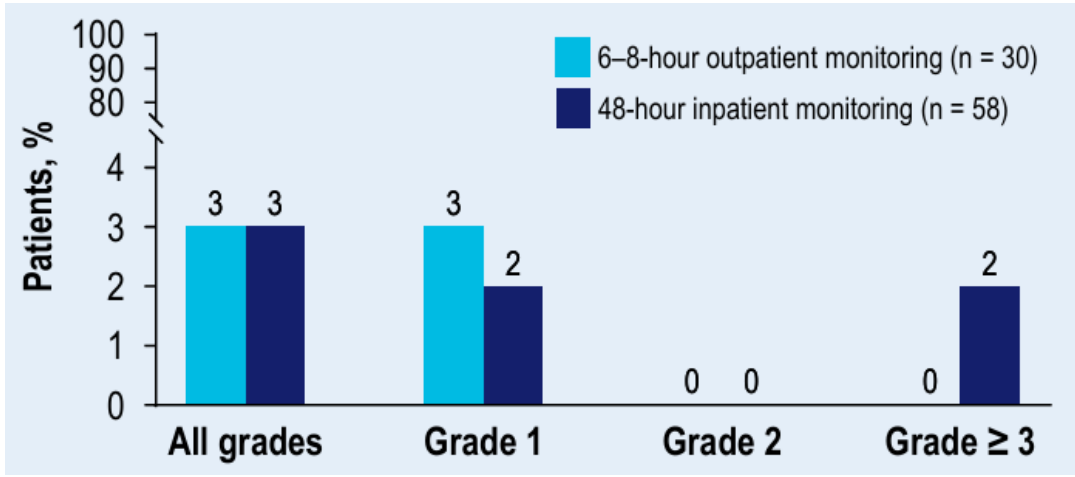
Monitored for ***48-hour in the inpatient*** setting in cycle 1 (n=58)

**For the outpatient monitoring group patients had to remain within 1 hour of the study site/hospital and having caregiver support 24 hours/day for 72 hours following tarlatamab administrations*

Cycle 1 **CRS** TRAEs by Grade



Cycle 1 **ICANS** TRAEs by Grade



Key Data

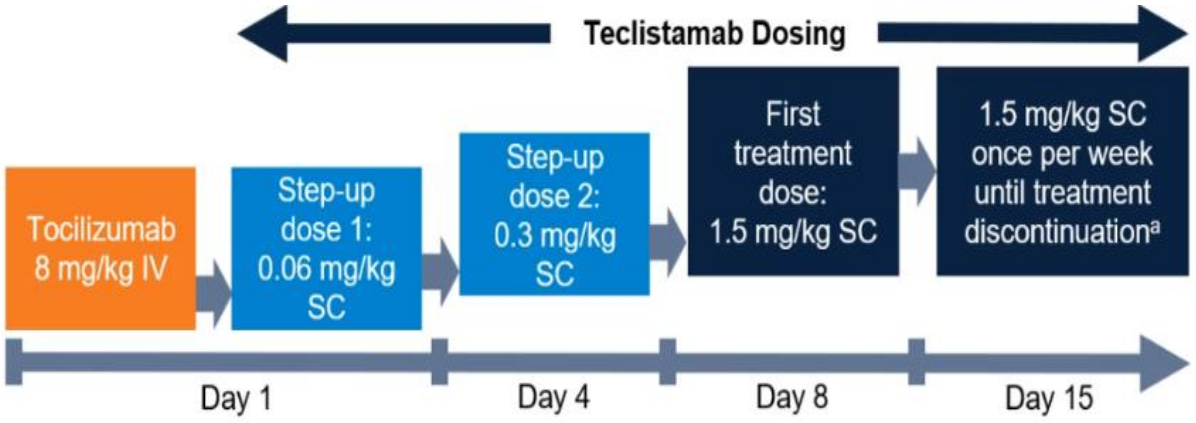
OPTec

A phase 2, non-randomized, single-arm study to evaluate outpatient (OP) step-up administration of teclistamab (Tec) in patients (pts) with RRMM

Rifkin R, et al. Poster presented at: 66th American Society of Hematology (ASH) Annual Meeting; December 7-10, 2024; San Diego, CA.

Study Design:

- 2 – 4 hrs before first step-up dose of teclistamab is administered patients receive a single dose of toci

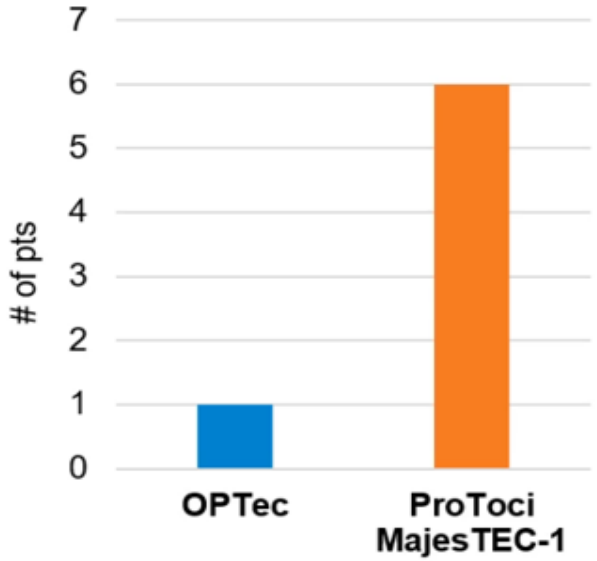


Abbreviations: IV, intravenous(ly); SC, subcutaneous(ly).
Note: Step-up dose 2 and the first treatment dose may be given between 3 to 5 days after step-up dose 1/2 and up to 7 days after step-up dose 1/2 to allow for resolution of adverse events.
[a]Dosing may be reduced to 1.5 mg/kg SC once every 2 weeks in patients who achieve partial response or better after 6 months of study treatment.

Primary Endpoint:

- Incidence of any-grade CRS in the first 2 cycles

CRS in OPTec versus ProToci cohort in MajesTEC-1



Abbreviations: CRS, cytokine release syndrome; ProToci, prophylactic tocilizumab; pt, patient.
Note: CRS occurred in 1 of 16 pts in OPTec and 6 of 24 pts (25%) in the ProToci cohort in MajesTEC-1.[1]

- Of 11 patients evaluable for response, 100% responded to therapy
  - 45% had either a stringent complete response (sCR) or complete response (CR)

Key Question

What are the key gaps in communication between academic and community centers regarding the use of bispecifics, and how can they be bridged?

Different EMR systems

Different protocols

Lack of communication

Lack of shared resources

Initiate standard referral pathways, share protocols and guidelines to maintain consistency

Assign care coordinator for regular case review

Equal access to training and resources for AE management

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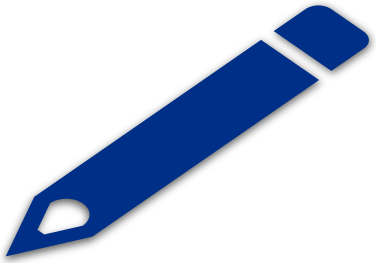
What are the key components to develop logistics and workflow for management?



Addition of BsAbs to the practice formulary

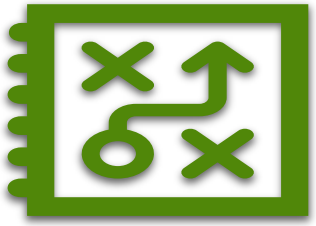
Identification of practice leaders willing to drive protocol development

Education of clinic and hospital staff who would manage patients treated with BsAbs

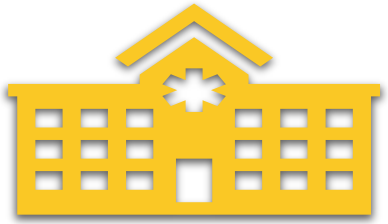
Understand patient support and provide patient education

Lines of communication between the treating practice, pharmacy, and hospital care staff before, during, and after treatment

Designate leads to oversee staff training



Create practice-specific management plans



Develop process for inpatient admission for moderate /severe CRS

What are the key components of a protocol?

Patient selection:

ECOG PS

Age

Comorbidities

Patient consent and education

Wallet card / information sheet

Talk to hospital:

Confirm patient candidacy for treatment

Arrangements for admission

Coordination with hospital staff

How is the bispecific given:

Subcutaneous or IV

Step-up dosing schedule

Location of step-up dosing inpatient or outpatient

What you need to start:

Blood pressure cuff, pulse ox, oral thermometer

CRS monitoring sheet

Confirmation of lodging

Caregiver or support person

Prophylactic meds

Rescue meds

Adverse event management:

CRS and ICANS

Manufacture protocol / hospital protocol

Awareness of timing of onset

Warning and precautions

Most common adverse events

Important phone numbers:

After hours on-call

Community practice Hem/Onc

Infusion clinic

Nurse coordinator

The more information the better!

Key Question

What best practices have you seen for ensuring a smooth transition of care when a patient moves between an academic and a community setting?

Operational challenges, delayed referral time

Length of time to get a patient into a hospital system

Getting patient back to the community

"Off the shelf" convenience

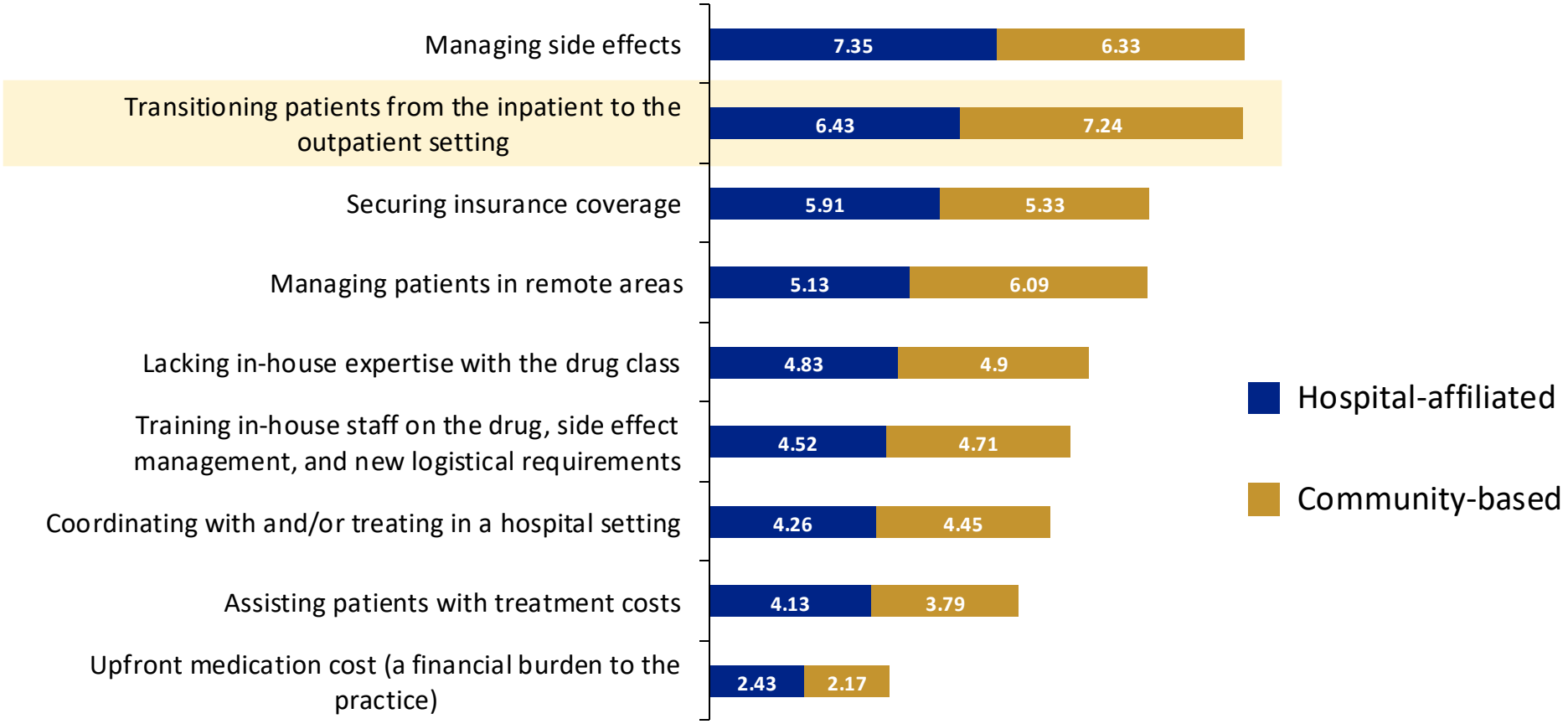
3 – 7 days for approval before 1st dose; time to "get ready"

Nurse coordinators

December 2024 Survey

Transitioning patients from the inpatient to the outpatient setting is viewed as a consistent barrier to using *bispecifics* in both the Hospital-affiliated and Community-based settings

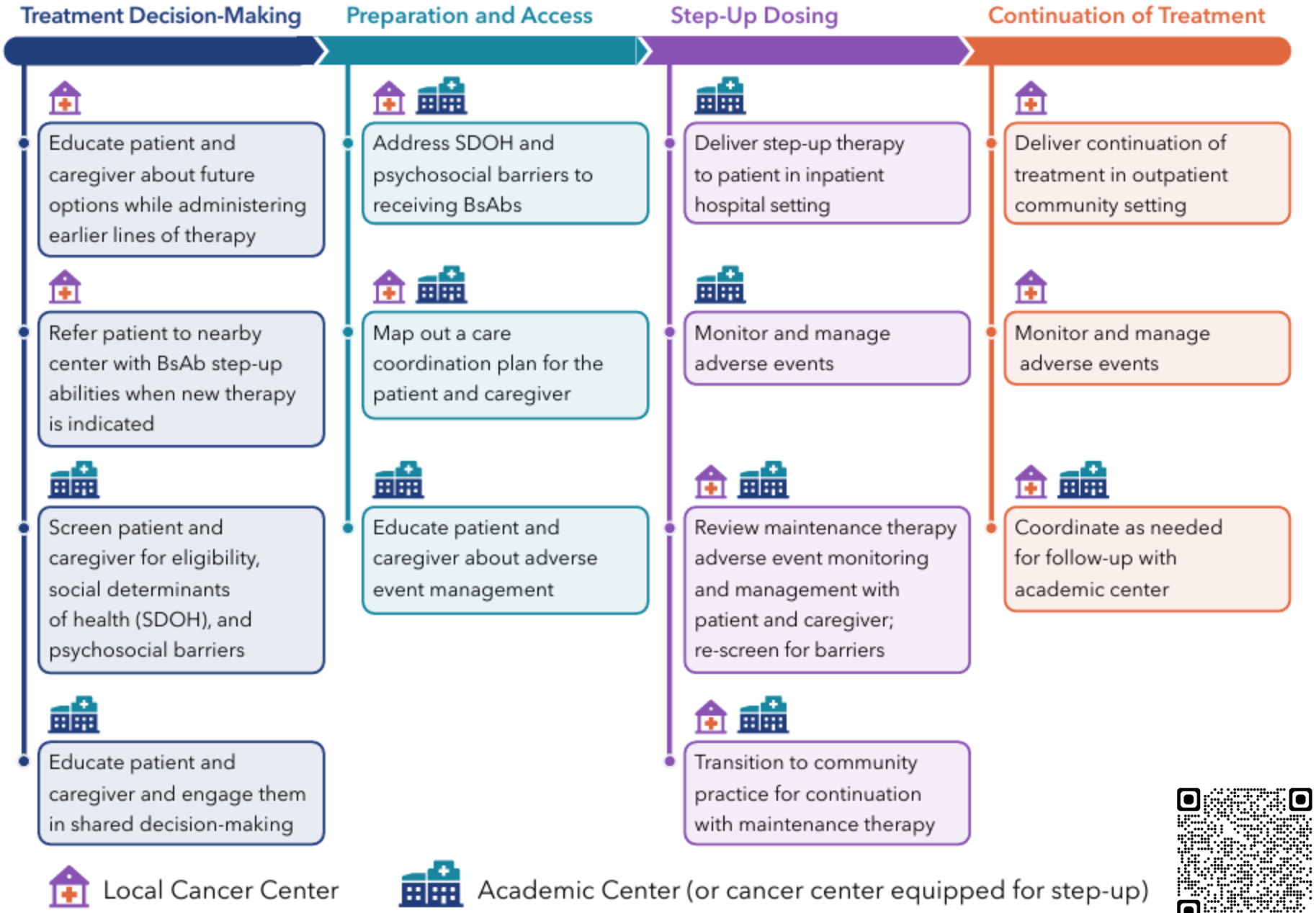
Rank the following barriers to using bispecific antibody therapies in order of significance.



n: 58 CB; 23 HA

Best practices…

How can a community cancer center and academic center partner to deliver BsAbs a patient?



https://cdn.sanity.io/files/0vv8moc6/accc-cancer/6ff749df8c110fd1e994d9a405cde79817f68d6b.pdf

Key Question

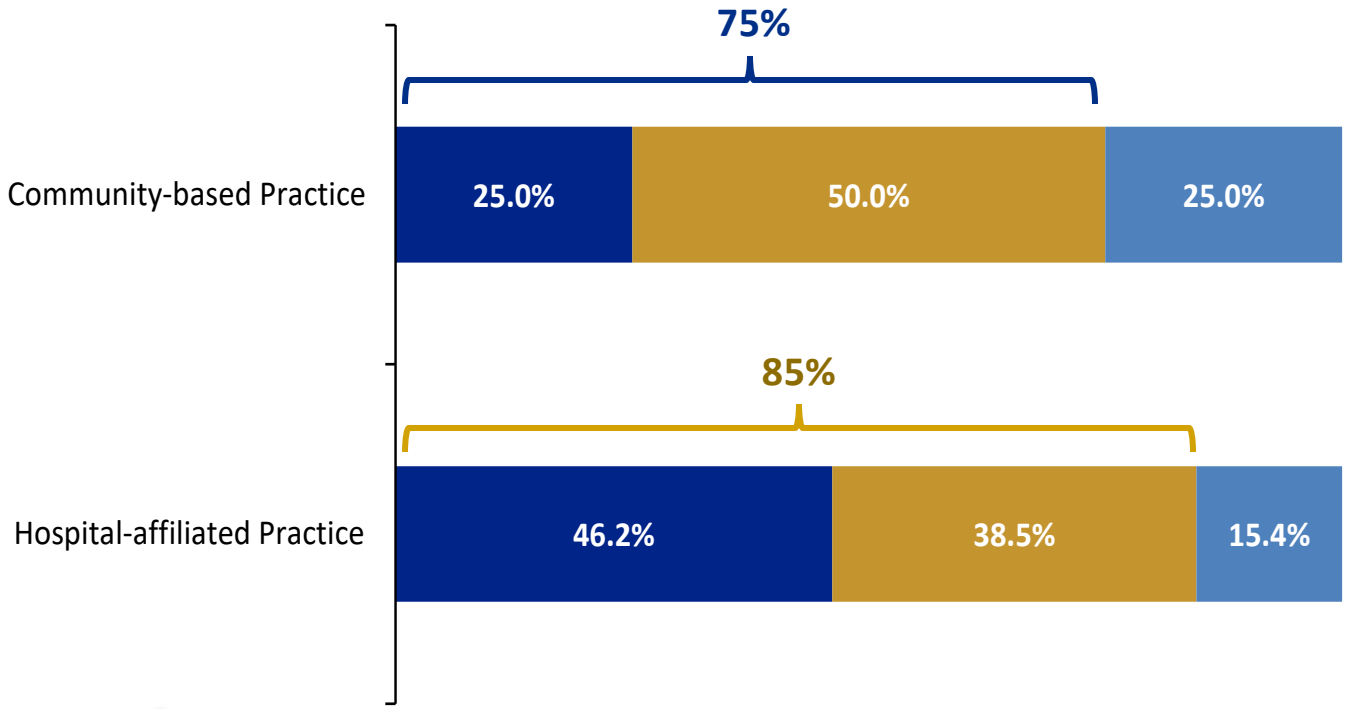
What best practices can you share for successfully implementing a bispecifics program and overcoming challenges?

- Form a multidisciplinary team (ecosystem) across academic and community setting
  - Oncologists, pharmacists, nursing, administrative staff
- Right patient selection, evidence based
  - Standard referral pathways with shared patient care coordinator
- Protocol development and patient monitoring guidelines
- Ongoing training and AE management with real world simulations
- Financial logistics; preauthorization and patient assistance programs
- Real world data collection; response and AE data to demonstrate program effectiveness

cornerstone specialty network™

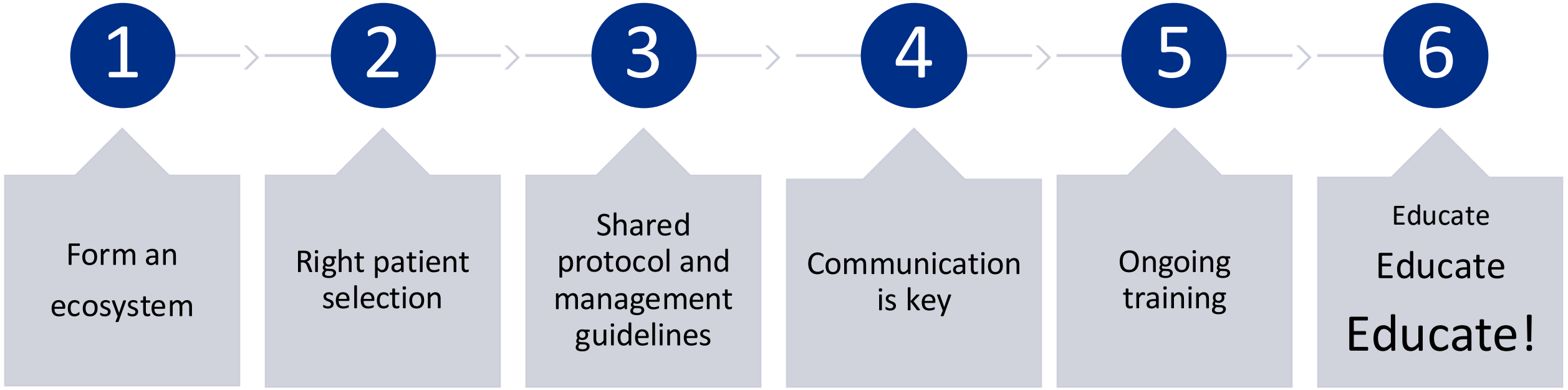
Of those that have implemented bispecific antibodies within their practices, most indicated that the integration of new bispecific antibodies has become easier over time.

How has the integration of bispecific antibody therapies into your clinical practice evolved over time?



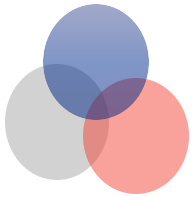
n: 32 CB; 13 HA

Key to Success

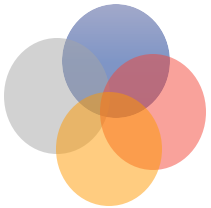


Beyond Bispecifics…?

Combining 3 or 4 or more different binding moieties has the potential of expanding new therapeutic options…Multiple clinical trials are underway…



Trispecifics?



Tetraspecifics?

Multispecifics?

When three is not a crowd: trispecific antibodies for enhanced cancer immunotherapy - PMC Theranostics 2023; 13(3): 1028-1041

Q & A

Thank you