Clearing Up Confusion Around “Bispecific Antibodies”

This page demystifies common confusion about “bispecific antibodies”—or, more precisely, bispecific T-cell engagers (BTCEs).

🔍 Clarifying “Bispecific” Terminology

⏳ Varying Observation Periods

💊 Different Supportive Care

🔍 Clarifying “Bispecific” Terminology

The **term “bispecific”** describes a mechanism of action—binding two different targets at the same time. But, as an all-encompassing drug class term, it is an inadequate oversimplification that **should be avoided**.

Why it matters: Not all bispecifics target T-cells! Non-T-cell-engaging bispecifics do NOT cause the same adverse reactions or require the same operational considerations as those that target T-cells.

- This distinction is vital for clinics developing **operational workflows**, as confusion can arise when comparing T-cell engaging with non-T-cell engaging agents.

We expect many more T-cell engaging and non-T-cell engaging therapies to be approved in the near future.

- As such, **knowing which ones engage T-cells is crucial**.

A closer look: Here is a list of bispecific therapies approved for hematology and oncology indications in the US as of August 2025.

Initial FDA Approval (Year)	Agent Name (Brand)	Targets	Cancer Type or Condition
T-cell Engaging			
2025	Linvoseltamab-gcpt (LYNOZYFIC™)	CD3 x BCMA	MM
2024	Tarlatamab-dlle (IMDELLTRA™)	CD3 x DLL3	SCLC
2023	Elranatamab-bcmm (ELREXFIO™)	CD3 x BCMA	MM
2023	Epcoritamab-bysp (EPKINLY®)	CD3 x CD20	LBCL
			FL
2023	Glofitamab-gxbm (COLUMVI™)	CD3 x CD20	LBCL
2023	Talquetamab-tgvs (TALVEY®)	CD3 x GPRC5D	MM
2022	Mosunetuzumab-axgb (LUNSUMIO™)	CD3 x CD20	FL
2022	Tebentafusp-tebn (KIMMTRAK®)	CD3 x gp100	HLA-A*02:01-positive uveal melanoma
2022	Teclistamab-cqyv (TECVAYLI®)	CD3 x BCMA	MM
2014	Blinatumomab (BLINCYTO®)	CD3 x CD19	B-ALL
Non-T-cell Engaging			
2024	Zanidatamab-hrii (ZIIHERA®)	HER2 x HER2	HER2-positive biliary tract cancer
2024	Zenocutuzumab-zbco (BIZENGRI®)	HER2 x HER3	NRG1 gene fusion positive NSCLC or pancreatic cancer
2021	Amivantamab-vmjw (RYBREVANT®)	EGFR x MET receptor	EGFR-mutated NSCLC
2017	Emicizumab-kxwh (HEMLIBRA®)	FIXa x FX	Hemophilia A

Abbreviations: B-ALL; B-cell acute lymphoblastic leukemia; BCMA, B-cell maturation antigen; CD3, cluster of differentiation 3; CD19, cluster of differentiation 19; CD20, cluster of differentiation 20; DLL3, delta-like ligand 3, EGFR, epidermal growth factor; EGFR, epidermal growth factor receptor; FIXa, activated factor IX; FX, factor X; FL, follicular lymphoma; GPRC5D, G protein-coupled receptor class C group 5 member D; HER2, human epidermal growth factor receptor 2; HER3, human epidermal growth factor receptor 3; HLA, human leukocyte antigen; LBCL, large B-cell lymphoma; MET, mesenchymal-epithelial transition; MM, multiple myeloma; NSCLC, non-small cell lung cancer; NRG1, neuregulin 1

⏳ Varying Observation Periods

Observation times can vary not just by drug and dose number, but also by indication.

Why it matters: It is crucial for the care team to be aware of the different observation times for BTCEs, as these recommendations vary by drug, dose number, and by indication.

Why the confusion? There are many elements of the varying observation periods that can be confusing.

- Some BTCEs do not require hospital monitoring during step-up dosing.
- For BTCEs that require hospitalization, some allow the first step-up dose to be administered in a clinic.
- The package insert (PI) recommends hospitalization for the full first dose of epcoritamab in large B-cell lymphoma but not for follicular lymphoma.
- Some PIs use the term “appropriate healthcare setting” for the place to administer BTCEs, providing looser language than “hospitalization.”

A closer look: Here are tables comparing observation periods for BTCEs (per their US PIs) based on cancer type.

- Abbreviations used in these tables:
    - FFD, first full dose
    - SUD, step-up dose

Leukemia BTCE

Blinatumomab			
Indication	MRD-positive B-cell Precursor ALL	r/r B-cell Precursor ALL	B-cell Precursor ALL in the Consolidation Phase
Step-Up Dosing	None	SUD 1: C1D1-C1D7 FFD: C1D8-C1D28	None
PI Recommendations for Hospitalization	C1: First 3 days C2: First 2 days Cycle = 42 days	C1: First 9 days C2: First 2 days Cycle = 42 days (changes to a 84-day cycle with cycles 6-9)	C1: First 3 days C2: First 2 days Cycle = 42 days
Duration of Infusion	Continuous infusion over 24 hours, 48 hours, 72 hours, 96 hours, or 7 days		

Lymphoma BTCEs

	Epcoritamab		Glofitamab	Mosunetuzumab
Indication	FL	LBCL	LBCL	FL
Step-Up Dosing	**3** SUDs SUD 1: C1D1 SUD 2: C1D8 SUD 3: C1D15 FFD: C1D22 Cycle = 28 days	**2** SUDs SUD 1: C1D1 SUD 2: C1D8 FFD: C1D15 Cycle = 28 days	**2** SUDs (After receiving obinutuzumab on C1D1) SUD 1: C1D8 SUD 2: C1D15 FFD: C2D1 Cycle = 21 days	**2** SUDs SUD 1: C1D1 SUD 2: C1D8 FFD: C1D15 Cycle = 21 days
PI Recommendations for Hospitalization	No	Patients should be hospitalized for **24 hours** after administration of the **FFD** (C1D15).	Administer infusions intravenously in a healthcare setting with immediate access to medical support to manage CRS, including severe CRS. Patients should be hospitalized for **24 hours** after completion of **SUD 1** (C1D8). Patients who experience any grade CRS during SUD 1 should be hospitalized during and for **24 hours** after completion of **SUD 2**.	No
Duration of Infusion	N/A		SUD 1 (C1D8): 4 hours SUD 2 (C1D15): 4 hours FFFD (C2D1): 4 hours C3-12: 2 hours Time of infusion may be extended up to 8 hours for patients who experience CRS with their previous dose of glofitamab.	C1: ≥4 hours C2+: 2 hours (if infusions from C1 were well-tolerated)

Multiple Myeloma BTCEs

	Elranatamab	Linvoseltamab	Talquetamab		Teclistamab
Step-Up Dosing	**2** SUDs SUD 1: C1D1 SUD 2: C1D4 FFD: C1D8	**2** SUDs SUD 1: C1D1 SUD 2: C1D8 FFD: C1D15	<u>Weekly Dosing</u> **2** SUDs SUD 1: C1D1 SUD 2: C1D4 FFD: C1D7	<u>Biweekly Dosing</u> **3** SUDs SUD 1: C1D1 SUD 2: C1D4 SUD 3: C1D7 FFD: C1D10	**2** SUDs SUD 1: C1D1 SUD 2: C1D4 FFD: C1D7
PI Recommendations for Hospitalization	Patients should be hospitalized for **48 hours** after administration of **SUD 1**, and for **24 hours** after administration of **SUD 2**. Patients should be **monitored** for **48 hours** following the next dose of elranatamab and should remain within proximity of a healthcare facility and consider hospitalization if they experience: • Grade 2 CRS or ICANS Patients should be **hospitalized** for **48 hours** following the next dose if they experience: • Grade 3 (1st occurrence) CRS or ICANS	Patients should be hospitalized for **24 hours** after administration of **SUD 1** and **SUD 2**. Patients should be **monitored** for **24 hours** following the next dose of linvoseltamab and should remain within proximity of a healthcare facility and consider hospitalization if they experience: • Grade 2 CRS or ICANS Patients should be **hospitalized** for **24 hours** following the next dose if they experience: • Grade 3 (1st occurrence) CRS or ICANS	Patients should be **hospitalized** for **48 hours** after administration of all doses within the step-up dosing period (All SUDs and FFD). Patients should be **hospitalized** for **48 hours** following the next dose if they experience: • Grade 2 CRS or ICANS • Grade 3 CRS (1st occurrence, duration <48 hours) • Grade 3 ICANS (1st occurrence)		Patients should be hospitalized for **48 hours** after administration of **all doses within the step-up dosing period** (SUDs and FFD). Patients should be **hospitalized** for **48 hours** following the next dose if they experience: • Grade 2 CRS or ICANS • Grade 3 CRS (1st occurrence, duration <48 hours) • Grade 3 ICANS (1st occurrence)
Duration of Infusion	N/A	SUD 1, 2 and FFD: 4 hours Weekly dosing: 1 hour for the second treatment dose, and 30 minutes for subsequent doses Biweekly and every 4 weeks dosing: 30 minutes	N/A		N/A

Small Cell Lung Cancer BTCE

Tarlatamab	
Step-Up Dosing	1 SUD SUD 1: C1D1 FFD: C1D8
PI Recommendations for Hospitalization	No specific mention of "hospitalization." Instead, the language "in an appropriate healthcare setting" is used.
PI Monitoring Recommendations	• C1D1 and C1D8: Monitor patients **from the start** of the tarlatamab administration for 22 to 24 hours in an appropriate healthcare setting. ○ Recommend that patients remain within 1-hour of an appropriate healthcare setting for a total of 48 hours from start of the infusion with tarlatamab, accompanied by a caregiver. • C1D15 and C2: Observe patients for 6-8 hours post tarlatamab infusion • C3-C4: Observe patients for 3-4 hours post tarlatamab infusion • C5+: Observe patients for 2 hours post tarlatamab infusion
Duration of Infusion	1 hour (Note: C1 also requires 1L of normal saline intravenously over 4-5 hours of post-administration)

Uveal Melanoma BTCE

Tebentafusp	
Step-Up Dosing	2 SUDs SUD 1: C1D1 SUD 2: C1D8 FFD: C1D15
PI Recommendations for Hospitalization	No specific mention of "hospitalization." Instead, the language "in an appropriate healthcare setting" is used.
PI Monitoring Recommendations	Administer the first **3 infusions** (SUD 1, SUD 2, and FFD) in an appropriate healthcare setting. Monitor patients during the infusion and for **at least 16 hours** after the infusion is complete.
Duration of Infusion	15-20 minutes

💊 Different Supportive Care

Supportive care with BTCEs is important for mitigating the risk of certain adverse events, such as CRS and infections.

Why it matters: Each BTCE has recommendations for empiric supportive care. Pre-administration medications—and sometimes post-administration medications—are used to reduce the risk of cytokine release syndrome. Infection prevention is also vital for certain therapies.

Why the confusion?

- Some, but not all, BTCEs recommend premedication with a corticosteroid, antihistamine, and antipyretic.
- Epcoritamab uniquely recommends 3 days of dexamethasone (or an equivalent corticosteroid) post-infusion for Cycle 1 and certain patients in Cycle 2.
- Corticosteroid doses vary among BTCEs and by indication.
- Inconsistencies exist between infection prophylaxis in package inserts and national guidelines.

A closer look: Here are tables comparing supportive care for BTCEs (per their US package inserts and national guidelines) based on cancer type.

Leukemia BTCE

Blinatumomab			
Indication	MRD-positive B-cell Precursor ALL	r/r B-cell Precursor ALL	B-cell Precursor ALL in the Consolidation Phase
Premedications	For adult patients: prednisone 100 mg IV or equivalent (e.g., dexamethasone 16 mg).	For adult patients: dexamethasone 20 mg IV or PO to the first dose of blinatumomab of each cycle, prior to a step dose (such as Cycle 1 Day 8), and when restarting an infusion after an interruption of 4 or more hours.	For adult patients: dexamethasone 20 mg IV prior to the first dose of blinatumomab of each cycle.
	For pediatric patients: dexamethasone 5 mg/m^2 (max dose: 20 mg) IV or PO prior to the first dose of blinatumomab in the first cycle and when restarting an infusion after an interruption of 4 or more hours in the first cycle.	For pediatric patients: dexamethasone 5 mg/m^2 (max dose: 20 mg) IV or PO prior to the first dose of blinatumomab in the first cycle, prior to a step dose (such as Cycle 1 Day 8), and when restarting an infusion after an interruption of 4 or more hours in the first cycle.	For pediatric patients: dexamethasone 5 mg/m^2 (max dose: 20 mg) IV or PO prior to the first dose of blinatumomab in the first cycle and when restarting an infusion after an interruption of 4 or more hours in the first cycle.
Postmedications	None	None	None
Prophylaxis			
Pneumocystis jirovecii pneumonia (PJP)	Consider		
Herpes virus	Consider		
Cytomegalovirus	No recommendation		
Tumor Lysis Syndrome	Recommend		
Intrathecal chemotherapy	Recommend		

Lymphoma BTCEs

	Epcoritamab	Glofitamab	Mosunetuzumab
Premedications	C1: • Dexamethasone (15 mg IV or PO) or Prednisolone (100 mg IV or PO) or equivalent • Diphenhydramine (50 mg IV or PO) or equivalent • Acetaminophen 650 mg to 1,000 mg PO	C1D8 + D15; C2; C3 • Dexamethasone 20 mg IV ○ If dexamethasone is not available, use prednisone 100 mg, prednisolone 100 mg, or methylprednisolone 80 mg IV • Antihistamine (diphenhydramine 50 mg IV or PO or equivalent) • Acetaminophen 500 mg to 1,000 mg PO	C1 + C2 • Dexamethasone 20 mg IV or methylprednisolone 80 mg IV • Diphenhydramine hydrochloride 50 mg to 100 mg or equivalent IV or PO antihistamine • Acetaminophen 500 mg to 1,000 mg PO
	C2+ (for patients who experienced G2 or G3 CRS with previous dose): • Dexamethasone (15 mg oral or intravenous) or Prednisolone (100 mg oral or intravenous) or equivalent	All Subsequent Infusions • Acetaminophen 500 mg to 1,0000 mg orally • Antihistamine (diphenhydramine 50 mg oral or intravenously or equivalent) • Patients who experienced any grade CRS with the previous dose: Dexamethasone 20 mg intravenously ○ If dexamethasone is not available, administer prednisone 100 mg, prednisolone 100 mg, or methylprednisolone 80 mg intravenously.	Cycles 3+ (Patients who experienced any grade CRS with the previous dose) • Dexamethasone 20 mg intravenous or methylprednisolone 80 mg intravenous • Diphenhydramine hydrochloride 50 mg to 100 mg or equivalent oral or intravenous antihistamine • Oral acetaminophen (500 mg to 1,000 mg)
Postmedications	C1 and C2+ (for patients who experienced G2 or G3 CRS with previous dose): • Dexamethasone (15 mg oral or intravenous) or Prednisolone (100 mg oral or intravenous) or equivalent for **3 consecutive days**	None	None
Prophylaxis			
Pneumocystis jirovecii pneumonia (PJP)	Recommend	PI: Consider Guidelines: Recommend	PI: Not mentioned Guidelines: Recommend
Herpes virus	PI: Consider Guidelines: Recommend	PI: Consider Guidelines: Recommend	PI: Not mentioned Guidelines: Recommend
Cytomegalovirus	PI: Not mentioned Guidelines: Consider	Consider	PI: Not mentioned Guidelines: Consider
Tumor Lysis Syndrome	Not mentioned	Recommended for patients at risk of tumor lysis syndrome; ensure adequate hydration status	Not mentioned
Other	N/A	Note: Since Obinutuzumab is given on C1D1, screening for hepatitis B virus is recommended. Treat as indicated	N/A

Multiple Myeloma BTCEs

	Elranatamab	Linvoseltamab	Talquetamab	Teclistamab
Premedications	During the SUD period (All SUDs and FFD). • Dexamethasone (or equivalent) 20 mg IV or PO • Diphenhydramine (or equivalent) 25 mg PO • Acetaminophen (or equivalent) 650 mg PO	During the SUD period (All SUDs and FFD), second treatment dose, and if indicated, subsequent treatment doses. • Dexamethasone (or equivalent) 40 mg IV before SUDs and FFD; once a treatment dose of linvoseltamab is tolerated without CRS and/or IRR with 40 mg (or equivalent), administer 10 mg dexamethasone (or equivalent) prior to the subsequent doses • Diphenhydramine (or equivalent) 25 mg PO • Acetaminophen (or equivalent) 650 mg to 1000 mg PO	During the SUD period (All SUDs and FFD). • Corticosteroid (dexamethasone 16 mg IV or PO, or equivalent) • Antihistamines (diphenhydramine 50 mg IV or PO, or equivalent) • Antipyretics (acetaminophen 650 mg to 1,000 mg IV or PO, or equivalent)	During the SUD period (All SUDs and FFD). • Corticosteroid (dexamethasone 16 mg IV or PO, or equivalent) • Antihistamines (diphenhydramine 50 mg IV or PO, or equivalent) • Antipyretics (acetaminophen 650 mg to 1,000 mg IV or PO, or equivalent)
Postmedications	None	None	None	None
Prophylaxis				
Pneumocystis jirovecii pneumonia (PJP)	Recommend	Recommended	Recommend	Recommend
Herpes virus	Recommend	Recommended	Recommend	Recommend
Cytomegalovirus	Consider	Consider	Consider	Consider
Tumor Lysis Syndrome	Not mentioned	Not mentioned	Not mentioned	Not mentioned

Small Cell Lung Cancer BTCE

	Tarlatamab
Premedications	C1D1 and C1D8 • Dexamethasone 8 mg IV (or equivalent)
Postmedications	C1 (all 3 doses) • 1 L of normal saline IV over 4-5 hours after completion of tarlatamab infusion
Prophylaxis	
Pneumocystis jirovecii pneumonia (PJP)	No
Herpes virus	No
Cytomegalovirus	No
Tumor Lysis Syndrome	No

Uveal Melanoma BTCE

Tebentafusp	
Premedications	No empiric premedication recommended • For moderate CRS that is persistent (lasting 2-3 hours) or recurrent, or for severe CRS, give a corticosteroid (e.g., dexamethasone 4 mg or equivalent) prior to the next dose.
Postmedications	No
Prophylaxis	
Pneumocystis jirovecii pneumonia (PJP)	No
Herpes virus	No
Cytomegalovirus	No
Tumor Lysis Syndrome	No

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