Comparison of Bispecific T-Cell Engagers (BTCEs)

Table 1. BTCEs in Lymphoma

Drug	Mosunetuzumab-axgb (LUNSUMIO®, LUNSUMIO VELO™) [1-3]		Epcoritamab-bysp (EPKINLY®) [4, 5]		Glofitamab-gxbm (COLUMVI™) [6, 7]
Manufacturer	Genentech, Inc.		AbbVie Inc. and Genmab US, Inc.		Genentech, Inc.
Target	CD3xCD20		CD3xCD20		CD3xCD20
Indication(s)	FL following 2 or more lines of therapy		(1) LBCL following 2 or more lines of therapy (2) FL following 2 or more lines of therapy		DLBCL following 2 or more lines of therapy
Route of Administration	IV (LUNSUMIO®) or SC (LUNSUMIO VELO™)		SC		IV
Dosing Schedule	C1: Days 1, 8, 15 C2+: Day 1, every 21 d, for up to 8 cycles for patients achieving CR; for up to 17 cycles for patients achieving PR or SD		C1-3: Days 1, 8 ,15, and 22 C4-9: Days 1 and 15 C10+: Day 1, every 28 d until progression		C1: Obinutuzumab, Day 1; glofitamab Days 8 and 15 C2-12: Day 1, every 21 d
CRS Mitigation					
SUD Schedule	**IV** C1D1: 1 mg C1D8: 2 mg C1D15: 60 mg (FFD)	**SC** C1D1: 5 mg C1D8: 45 mg (FFD) C1D15: 45 mg	**LBCL** CD1: 0.16 mg C1D8: 0.8 mg C1D15: 48 mg (FFD) C1D22: 48 mg	**FL** C1D1: 0.16 mg C1D8: 0.8 mg C1D15: 3 mg C1D22: 48 mg (FFD)	C1D1: Obinutuzumab C1D8: 2.5 mg (first dose of glofitamab) C1D15: 10 mg C2D1+: 30 mg (FFD)
Premedications	(1) Acetaminophen 500–1,000 mg (2) Diphenhydramine 50–100 mg (or equivalent) (3) Dexamethasone 20 mg or methylprednisolone 80 mg Note: Premedications are recommended for IV mosunetuzumab during C1 and C2 and for SC administration during C1 only. Regardless of route of administration, any patient who experienced CRS of any grade with the previous dose should receive premedications prior to the next dose.		(1) Acetaminophen 650–1,000 mg (2) Diphenhydramine 50 mg (or equivalent) (3) Dexamethasone 15 mg or prednisolone 100 mg (or equivalent), before C1 treatments and for 3 consecutive days after. Continue dexamethasone thereafter if G2 or G3 CRS with prior dose		(1) Acetaminophen 500–1,000 mg (2) Diphenhydramine 50 mg (or equivalent) (3) Dexamethasone 20 mg (or equivalent) on C1D8, C1D15, C2D1, and C3D1. Continue if CRS occurs with prior dose
Hospitalization	Consider		LBCL: C1D15 (FFD): 24-h admission FL: Consider		C1D8: 24-h admission

<table>
<tr><th>Drug</th><th colspan="5">Mosunetuzumab-axgb (LUNSUMIO®, LUNSUMIO VELO™) [1-3]</th><th colspan="6">Epcoritamab-bysp (EPKINLY®) [4, 5]</th><th colspan="5">Glofitamab-gxbm (COLUMVI™) [6, 7]</th></tr>
<tr><td rowspan="4">CRS Incidence</td><td>G1</td><td>G2</td><td>G3</td><td>G4</td><td>G5</td><td></td><td>G1</td><td>G2</td><td>G3</td><td>G4–5</td><td>G1</td><td>G2</td><td>G3</td><td>G4</td><td>G5</td></tr>
<tr><td rowspan="2">26%</td><td rowspan="2">17%</td><td rowspan="2">1%</td><td rowspan="2">1%</td><td rowspan="2">0%</td><td>LBCL</td><td>37%</td><td>17%</td><td>3%</td><td>0%</td><td rowspan="2">47%</td><td rowspan="2">12%</td><td rowspan="2">3%</td><td rowspan="2">1%</td><td rowspan="2">0%</td></tr>
<tr><td>FL</td><td>45%</td><td>9%</td><td>0%</td><td>0%</td></tr>
<tr><td colspan="2">Time course for CRS onset</td><td colspan="3">Median time to CRS onset</td><td colspan="3">Time course for CRS onset</td><td colspan="3">Median time to CRS onset</td><td colspan="3">Time course for CRS onset</td><td colspan="2">Median time to CRS onset</td></tr>
<tr><td colspan="2">C1D1: 23%
C1D8: 6%
C1D15: 36%
C2D1: 10%
C3+D1: 2%</td><td colspan="3">C1D1: 5 h
C1D8: 20 h
C1D15: 27 h
C2D1: 38 h</td><td colspan="3"><table><tr><td></td><td>LBCL</td><td>FL</td></tr><tr><td>C1D1</td><td>6%</td><td>12%</td></tr><tr><td>C1D8</td><td>12%</td><td>6%</td></tr><tr><td>C1D15</td><td>43%</td><td>15%</td></tr><tr><td>C1D22</td><td>5%</td><td>37%</td></tr></table></td><td colspan="3"><table><tr><td></td><td>LBCL</td><td>FL</td></tr><tr><td>After most recent dose</td><td>24 h (range: 0–10d)</td><td>59 h (range: 0.1–7d)</td></tr><tr><td>After FFD</td><td>21 h (range: 0–7 d)</td><td>61 h (range: 0.1–7d)</td></tr></table></td><td colspan="3">C1D8: 42%
C1D15: 25%
C2: 26%
C3+: 1%</td><td colspan="2">C1D8: 14 h (range: 6–52 h)</td></tr>
<tr><td>Median Duration of CRS</td><td colspan="5">3 d (range: 1–29 d)</td><td colspan="6">2 d (range: 1–27 d)</td><td colspan="5">31 h (range: 0.5–317 h)</td></tr>
<tr><td rowspan="3">ICANS Incidence</td><td colspan="2">G1–2</td><td colspan="3">G3–5</td><td></td><td>G1</td><td>G2</td><td>G3</td><td>G4–5</td><td colspan="2">G1–2</td><td colspan="2">G3–4</td><td>G5</td></tr>
<tr><td colspan="2" rowspan="2">3%</td><td colspan="3" rowspan="2">0%</td><td>LBCL</td><td>5%</td><td>1%</td><td>0%</td><td>0.6%</td><td colspan="2" rowspan="2">5%</td><td colspan="2" rowspan="2">3%</td><td rowspan="2">0%</td></tr>
<tr><td>FL</td><td>4%</td><td>2%</td><td>0%</td><td>0%</td></tr>
<tr><td>Any Grade Adverse Events (with >25% Incidence)</td><td colspan="5">Lymphopenia (84%–100%), hypophosphatemia (48%–78%), anemia (60%–68%), leukopenia (60%), neutropenia (50%–58%), thrombocytopenia (33%–46%), CRS (30%–44%), fatigue (39%–42%), hyperglycemia (42%), rash (35%–39%), increased AST (28%–39%), hypomagnesemia (25%–34%), hypokalemia (27%–33%), increased ALT (32%–34%), headache (17%–32%), pyrexia (11%–29%), hyperuricemia (22% to 28%), musculoskeletal pain (20%–28%)</td><td colspan="6">Lymphopenia (87%–94%), anemia (59%–62%), hyponatremia (51%–56%), hypophosphatemia (LBCL: 56%), injection site reactions (FL: 58%; LBCL: 27%), leukopenia (53%–58%), neutropenia (50%–55%), CRS (49%–51%), thrombocytopenia (48%–49%), increased AST (44%–48%), increased ALT (45%–47%), serious infection (FL: 40%; LBCL: 15%), hypercreatininemia (FL: 36%; LBCL: 24%), fatigue (29%–37%), upper respiratory tract infection (FL: 29%; LBCL: <10%), skin rash (FL: 28%; LBCL: 15%), hypokalemia (FL: 20%; LBCL: 34%), increased ALP (FL: 29%), hyperbilirubinemia (FL: 28%), hypomagnesemia (FL: 20%; LBCL: 31%), musculoskeletal pain (28%), pyrexia (24%–26%), diarrhea (20%–26%)</td><td colspan="5">Lymphopenia (90%), hypofibrinogenemia (84%), anemia (72%), CRS (70%), hypophosphatemia (69%), neutropenia (56%), thrombocytopenia (56%), hyponatremia (49%), hypocalcemia (48%), increased GGT (33%), hypokalemia (32%)</td></tr>
<tr><td>Grade 3 or > Adverse Events (with >25% Incidence)</td><td colspan="5">Lymphopenia (22%–98%), hypophosphatemia (46%), hyperglycemia (42%), neutropenia (26%–40%)</td><td colspan="6">Lymphopenia (77%–82%), neutropenia (14%–32%)</td><td colspan="5">Lymphopenia (83%), hypophosphatemia (28%), neutropenia (26%)</td></tr>
<tr><td>REMS Program</td><td colspan="5">No</td><td colspan="6">No</td><td colspan="5">No</td></tr>
<tr><td>Initial Approval</td><td colspan="5">December 2022</td><td colspan="6">May 2023 (LBCL), June 2024 (FL)
Note: See Table 4 for information on epcoritamab in combination with lenalidomide and rituximab</td><td colspan="5">June 2023</td></tr>
<tr><td>Pivotal Trial(s)</td><td colspan="5">GO29781</td><td colspan="6">EPCORE NHL-1</td><td colspan="5">NP30179</td></tr>
</table>

Table 2 (1 of 2). BTCEs in Multiple Myeloma

Drug	Teclistamab-cqyv (TECVAYLI®) [8, 9]				Talquetamab-tgvs (TALVEY®) [10, 11]			
Manufacturer	Janssen Biotech, Inc.				Janssen Biotech, Inc.			
Target	CD3xBCMA				CD3xGPRC5D			
Indication(s)	MM following 4 or more lines of therapy				MM following 4 or more lines of therapy			
Route of Administration	SC				SC			
Dosing Schedule	C1: Days 1, 4, 7 C2+: Weekly until progression For patients who have achieved and maintained a CR or better for >6 mo, consider biweekly dosing				**Weekly Dosing** C1: Days 1, 4, 7 C2+: Weekly until progression		**Biweekly Dosing** C1: Days 1, 4, 7, 10 C2+: Every 2 weeks until progression	
CRS Mitigation								
SUD Schedule	C1D1: 0.06 mg/kg C1D3: 0.3 mg/kg C1D5: 1.5 mg/kg (FFD)				**Weekly Dosing** C1D1: 0.01 mg/kg C1D4: 0.06 mg/kg C1D7: 0.4 mg/kg (FFD)		**Biweekly Dosing** C1D1: 0.01 mg/kg C1D4: 0.06 mg/kg C1D7: 0.4 mg/kg C1D10: 0.8 mg/kg (FFD)	
Premedications	(1) Acetaminophen 650–1,000 mg (or equivalent) for C1 (2) Diphenhydramine 50 mg (or equivalent) for C1 (3) Dexamethasone 16 mg for C1				(1) Acetaminophen 650–1,000 mg (or equivalent) for C1 (2) Diphenhydramine 50 mg (or equivalent) for C1 (3) Dexamethasone 16 mg (or equivalent) for C1			
Hospitalization	All SUDs and FFD: 48-h admission				All SUDs and FFD: 48-h admission			
CRS Incidence	**G1**	**G2**	**G3**	**G4–5**	**G1**	**G2**	**G3**	**G4–5**
	50%	21%	1%	0%	57%	17%	2%	0%
	Time course for CRS onset		**Median time to CRS onset**		**Time course for CRS onset**		**Median time to CRS onset**	
	C1D1: 42% C1D3: 35% C1D5: 24% Subsequent doses: <3%		All doses: 2 d (range: 1–6 d)		**Weekly Dosing** C1D1: 29% C1D4: 44% C1D7: 30% **Biweekly Dosing** C1D7: 33% C1D10: 12%		All doses: 27 h (range: 0.1–167 h)	
Median Duration of CRS	2 d (range: 1–9 d)				17 h (range: 1–622 h)			
ICANS Incidence	Any grade: 6%				Any grade: 9%			
Any Grade Adverse Events (with >25% Incidence)	Lymphopenia (92%), leukopenia (86%), neutropenia (84%), pyrexia (76%), CRS (72%), thrombocytopenia (71%), hypoalbuminemia (68%), anemia (67%), neurotoxicity (57%), musculoskeletal pain (44%), increased ALP (42%), hypophosphatemia (38%), increased GGT (37%), injection-site reaction (37%), hyponatremia (35%), increased AST (34%), fatigue (33%), hypocalcemia (31%), hypercreatininemia (30%), infection (30%), diarrhea (29%), increased ALT (28%), upper respiratory tract infection (26%), nausea (25%), headache (25%)				Lymphopenia (90%), pyrexia (83%), CRS (76%), leukopenia (73%), dysgeusia (49%–70%), anemia (67%), neutropenia (64%), weight loss (35%–62%), thrombocytopenia (62%), hypoalbuminemia (66%), neurotoxicity (55%), nail disorder (50%), increased ALP (49%), hypophosphatemia (44%), musculoskeletal pain (43%), skin disorder (41%), rash (38%), increased GGT (38%), fatigue (37%), xerostomia (34%), increased ALT (33%), increased AST (31%), hypokalemia (31%), hyponatremia (31%), xerosis (30%)			

Drug	Teclistamab-cqyv (TECVAYLI®) [8, 9]	Talquetamab-tgvs (TALVEY®) [10, 11]
Grade 3 or > Adverse Events (with >25% Incidence)	Neutropenia (64%), anemia (37%), lymphopenia (32%)	Lymphopenia (80%), leukopenia (35%), neutropenia (35%), anemia (30%)
REMS Program	Yes	Yes
Initial Approval	October 2022	August 2023
Pivotal Trial(s)	MajesTEC-1	MonumenTAL-1

Table 2 (2 of 2). BTCEs in Multiple Myeloma

Drug	Elranatamab-bcmm (ELREXFIO®) [12, 13]	Linvoseltamab-gcpt (LYNOZYFIC™) [14, 15]
Manufacturer	Pfizer	Janssen Biotech, Inc.
Target	CD3xBCMA	CD3xGPRC5D
Indication(s)	MM following 4 or more lines of therapy	MM following 4 or more lines of therapy
Route of Administration	SC	IV
Dosing Schedule	C1: Days 1, 4, 8 C2+: Weekly through Week 24 Weeks 25–48 (in patients achieving a PR or better at 24 weeks with response maintained for ≥2 months): Biweekly Week 49+ (for patients who have maintained the response following 24 weeks of treatment at the biweekly dosing schedule): Every 4 wk	C1: Days 1, 8, 15 C2+: Weekly through Week 13 Week 14+: Biweekly Week 24+ (for patients who have achieved and maintained VGPR or better at or after Week 24 and received at least 17 doses of 200 mg): Every 4 wk
CRS Mitigation		
SUD Schedule	C1D1: 12 mg C1D4: 32 mg C1D8: 76 mg (FFD)	C1D1: 5 mg C1D8: 25 mg C1D15: 200 mg (FFD)
Premedications	(1) Acetaminophen 650 mg (or equivalent) for C1 (2) Diphenhydramine 25 mg (or equivalent) for C1 (3) Dexamethasone 20 mg (or equivalent) for C1	(1) Acetaminophen 650–1000 mg (or equivalent) for SUDs and first and second treatment doses (2) Diphenhydramine 25 mg (or equivalent) for SUDS and first and second treatment doses (3) Dexamethasone 40 mg (or equivalent) for SUDs and first treatment dose Once tolerated without CRS or infusion-related reactions, 10 mg dexamethasone (or equivalent) prior to the subsequent treatment dose
Hospitalization	C1D1: 48-h admission C1D4: 24-h admission	C1D1 and C1D8: 24-h admission
CRS Incidence	**G1** / **G2** / **G3** / **G4–5** 44% / 14% / 1% / 0%	**G1** / **G2** / **G3** / **G4–5** 35% / 10% / 1% / 0%
	Time course for CRS onset C1D1: 43% C1D4: 19% C1D8: 7% C2D1: 2%	**Median time to CRS onset** All doses: 2 d (range: 1–9 d)
	Time course for CRS onset C1D1: 38% C1D8: 17% C1D15: 10% C2D1: 4%	**Median time to CRS onset** All doses: 11 h (range: -1–184 h)
Median Duration of CRS	2 d (range: 1–19 d)	15 h (range: 1–76 h)
ICANS Incidence	Any grade: 3%	Any grade: 8%

Drug	Elranatamab-bcmm (ELREXFIO®) [12, 13]	Linvoseltamab-gcpt (LYNOZYFIC™) [14, 15]
Any Grade Adverse Events (with >25% Incidence)	Lymphopenia (91%), leukopenia (69%), anemia (68%), neutropenia (62%), thrombocytopenia (61%), neurotoxicity (59%), CRS (13%–58%), hypoalbuminemia (55%), fatigue (43%), severe infection (42%), increased AST (40%), hypercreatininemia (38%), injection-site reaction (37%), hypokalemia (36%), diarrhea (36%), increased ALT (36%), upper respiratory tract infection (36%), musculoskeletal pain (34%), increased ALP (34%), decreased CrCl (32%), pneumonia (25%–32%), decreased appetite (26%), skin rash (26%)	Lymphopenia (97%), anemia (72%), thrombocytopenia (64%), leukopenia (63%), neutropenia (62%), increased AST (61%), increased ALT (46%), hypophosphatemia(55%), neurotoxicity (54%), musculoskeletal pain (53%), hypercreatininemia (47%), CRS (46%), serious infection (42%), cough (39%), upper respiratory tract infection (35%), diarrhea (35%), fatigue (34%), pneumonia (28%)
Grade 3 or > Adverse Events (with >25% Incidence)	Lymphopenia (84%), neutropenia (51%), anemia (43%), leukopenia (40%), thrombocytopenia (32%)	Lymphopenia (92%), neutropenia (47%), anemia (42%), leukopenia (31%)
REMS Program	Yes	Yes
Initial Approval	August 2023	July 2025
Pivotal Trial(s)	MagnetisMM-3	LINKER-MM1

Table 3. BTCEs in Other Indications

Drug	Blinatumomab (BLINCYTO®) [16-19]	Tebentafusp-tebn (KIMMTRAK®) [20, 21]	Tarlatamab-dlle (IMDELLTRA®) [22-24]
Manufacturer	Amgen, Inc.	Immunocore Commercial LLC	Amgen, Inc.
Target	CD3xCD19	CD3xgp100peptide-HLA	CD3xDLL3
Indication(s)	(1) MRD+ BCP-ALL (2) R/R BCP-ALL (3) BCP-ALL in the consolidation phase	HLA-A*02:01-positive unresectable or metastatic uveal melanoma	ES-SCLC following progression on platinum-based chemotherapy
Route of Administration	IV	IV	IV
Dosing Schedule	**MRD+ BCP-ALL and BCP-ALL in consolidation phase** Induction Cycle 1: Days 1–28 then 14 d off Consolidation Cycles 2–4: Days 1–28 then 14 d off **R/R BCP-ALL** Induction C1 and C2: Days 1–28 then 14 days off Consolidation C3–5: Days 1–28 then 14 days off Continued Therapy C6–9: Days 1–28 then 56 days off	Once weekly until progression	C1: Days 1, 8 ,15 C2+: Days 1 and 15; every 28 d until progression
CRS Mitigation			
SUD Schedule	**R/R BCP-ALL,** Induction Cycle 1: Days 1–7: 9 mcg/d Days 8–28: 28 mcg/d Note: See PI for dosing for patients under 45 kg	D1: 20 mcg D8: 30 mcg D15: 68 mcg (FFD)	C1D1: 1 mg C1D8: 10 mg (FFD) C1D15: 10 mg
Premedications	**MRD+ BCP-ALL and BCP-ALL in consolidation phase** Corticosteroid: Prednisone 100 mg (or equivalent) D1 in each cycle **For adults with R/R BCP-ALL** Corticosteroid: Dexamethasone 20 mg D1 in each cycle, prior to a step-up dose, and when restarting an infusion after interruption of ≥4 h	None	(1) Dexamethasone 8 mg (or equivalent) on C1D1 and C1D8 (2) 1L NS IV over 4–5 h immediately after infusion completion on C1D1, C1C8, and C1D15
Hospitalization	**MRD+ BCP-ALL and BCP-ALL in consolidation phase:** C1 (3 d) and C2 (2 d) **R/R BCP-ALL:** C1 (9 d), C2 (2 d)	D1, D8, and D15: 16 h monitoring Monitoring should be done in an appropriate healthcare setting	C1D1, C1D8: 22–24 h monitoring C1D15: 6–8 h monitoring Subsequent infusions: 2 h monitoring Monitoring should be done in an appropriate healthcare setting

Drug	Blinatumomab (BLINCYTO®) [16-19]		Tebentafusp-tebn (KIMMTRAK®) [20, 21]				Tarlatamab-dlle (IMDELLTRA®) [22-24]				
CRS Incidence	**MRD+ BCP-ALL** (any grade): 15% **R/R BCP-ALL** (any grade): 7% **BCP-ALL in consolidation phase** (any grade): 16%		**G1**	**G2**	**G3**	**G4-5**	**G1**	**G2**	**G3**	**G4**	**G5**
			12%	76%	1%	0%	34%	19%	1%	0.5%	0%
	Time course for CRS onset	**Median time to CRS onset**	**Time course for CRS onset**		**Median time to CRS onset**		**Time course for CRS onset**		**Median time to CRS onset**		
	Not reported	All doses: 2 d	Day 1: 85% Day 8: 75% Day 15: 60% Day 22: 30% Day 29: 10%		All doses: Within the day of the infusion		C1D1: 39% C1D8: 28% C1D15: 6% C1D1: 2%		All doses: 14 h (range: 1–268 h)		
Median Duration of CRS	5 d		2 d				4 d (IQR 2–6 d)				
ICANS Incidence	Any grade: 8%		N/A				**G1**	**G2–4**	**G5**		
							5%	4%	0%		
Any Grade Adverse Events (with >25% Incidence)	Pyrexia (55%–91%), lymphocytopenia (80%), infusion-related reactions (30%–77%), headache (23%–39%), neurotoxicity (65%), infections (28%–39%), tremor (31%), neutropenia (15%–31%), anemia (infants, children, adolescents: 41%; adults: 24%–25%), chills (28%), thrombocytopenia (infants, children, adolescents: 34%; adults: 10%–21%), hypertension (infants, children, adolescents: 26%; adults: 8%)		Lymphocytopenia (91%), CRS (89%), hypercreatininemia (87%), skin rash (83%), pyrexia (76%), pruritus (69%), hyperglycemia (66%), increased ALT (≤65%), increased AST (≤65%), fatigue (64%), anemia (51%), hypophosphatemia (51%), chills (48%), hypoalbuminemia (47%), hypocalcemia (45%), abdominal pain (45%), edema (45%), nausea (49%), hypotension (39%), hyperlipasemia (37%), hypomagnesemia (34%), increased ALP (34%), antibody development (29%–33%), headache (31%), xeroderma (31%), vomiting (30%), hyponatremia (30%), hyperkalemia (29%), hypopigmentation (28%), skin edema (27%), hyperbilirubinemia (27%), diarrhea (25%), erythema of skin (24%–25%)				Lymphocytopenia (65%–84%), neurotoxicity (≤65%), hyponatremia (57%–68%), CRS (55%–56%), anemia (51%–58%), fatigue (39%–51%), leukopenia (44%–50%), hypokalemia (41–50%), increased AST (40%–44%), increased ALT (32%–42%), infection (43%), pyrexia (29%–36%), decreased appetite (34%–37%), dysgeusia (28%–36%), thrombocytopenia (25%–33%), hypomagnesemia (21–33%), musculoskeletal pain (27%–30%), constipation (30%), hypercreatininemia (23%–29%), hypernatremia (26%–35%), prolonged PTT (26%), nausea (22%–25%)				
Grade 3 or > Adverse Events (with >25% Incidence)	Lymphocytopenia (80%), neutropenia (15% to 28%)		Lymphocytopenia (56%)				Lymphocytopenia (27%–57%)				
REMS Program	No		No				No				
Initial Approval	December 2014		January 2022				May 2024				
Pivotal Trial(s)	BLAST, TOWER, ECOG-ACRIN E1910		IMCgp100-202				DeLLphi-301, DeLLphi-304				

Table 4 (1 of 2). BTCEs in Combination Regimens

<table>
<tr><th>Combination</th><th colspan="4">Epcoritamab-bysp (EPKINLY®) and R² (Lenalidomide and Rituximab) [25]</th><th colspan="3">Teclistamab-cqyv (TECVAYLI®) and Talquetamab-tgvs (TALVEY®) [26, 27]</th></tr>
<tr><td>Indication(s)</td><td colspan="4">FL following 1 or more lines of therapy</td><td colspan="3">MM following 4 or more lines of therapy</td></tr>
<tr><td>Dosing Schedule</td><td colspan="4">Cycle length: 28 d
Epcoritamab: C1-3: Day 1, 8, 15, and 22; C4-12: Day 1
Lenalidomide: C1-12: QD, Days 1-21
Rituximab: C1: Day 1, 8, 15, 22; C2-5: Day 1</td><td colspan="3">Cycle length: 28 d
C1: 3 SUDs administered 2–4 days apart and prior to FFD
C2: Teclistamab and talquetamab biweekly
C4+ (if PR or better is achieved): Teclistamab and talquetamab monthly until progression</td></tr>
<tr><td colspan="8">CRS Mitigation</td></tr>
<tr><td>SUD Schedule</td><td colspan="4">C1D1: 0.16 mg
C1D8: 0.8 mg
C1D15: 3 mg
C1D22: 48 mg (FFD)</td><td colspan="3">SUD | Talquetamab | Teclistamab
SUD 1 | 0.01 mg/kg | 0.06 mg/kg
SUD 2 | 0.06 mg/kg | 0.3 mg/kg
SUD 3 | 0.4 mg/kg | 1.5 mg/kg
FFD | 0.8 mg/kg | 3 mg/kg</td></tr>
<tr><td>Premedications</td><td colspan="4">(1) Acetaminophen 650–1,000 mg
(2) Diphenhydramine 50 mg (or equivalent)
(3) Dexamethasone 15 mg or prednisolone 100 mg (or equivalent), before C1 treatments and for 3 consecutive days after

Continue dexamethasone thereafter if G2 or G3 CRS with prior dose</td><td colspan="3">Teclistamab is administered before talquetamab.

(1) Acetaminophen 650–1,000 mg (or equivalent) for C1
(2) Diphenhydramine 50 mg (or equivalent) for C1
(3) Dexamethasone 16 mg for C1</td></tr>
<tr><td>Hospitalization</td><td colspan="4">Consider</td><td colspan="3">For 48 h after administration of all SUDs and FFD</td></tr>
<tr><td>CRS Incidence</td><td>G1</td><td>G2</td><td>G3</td><td>G4</td><td>G1-2</td><td>G3</td><td>G4-5</td></tr>
<tr><td></td><td>19%</td><td>5%</td><td>12%</td><td>0%</td><td>77%</td><td>2%</td><td>0%</td></tr>
<tr><td></td><td colspan="2">Time course for CRS onset</td><td colspan="2">Median time to CRS onset</td><td colspan="3" rowspan="2">Median time to onset and duration of CRS were 2 days each.</td></tr>
<tr><td></td><td colspan="2">C1D1: 5%
C1D8: 4%
C1D15: 2%
C1D22: 18%</td><td colspan="2">From the most recent dose: 78 h (range: 0.2–12 d)

After the FFD: 41 h (range: 0.3–12 d)</td></tr>
<tr><td>ICANS Incidence</td><td colspan="4">Any grade: 1%</td><td colspan="3">Any grade: 3% (G3: 1%)</td></tr>
<tr><td>What is Different Between the Single Agent(s) and Combination Therapy?</td><td colspan="4">• When epcoritamab is used as a single agent for FL, it is continued until disease progression or unacceptable toxicity. When used with R², treatment is continued for a total of 12 cycles or until disease progression or unacceptable toxicity, whichever occurs first.
• CRS occurred in less patients when used in combination with R² (26%) versus monotherapy (49%).
• When epcoritamab is used in combination with R², dosing shifts to once per cycle beginning in Cycle 4, with administration only on Day 1 for Cycles 4 and beyond.</td><td colspan="3">• Step up dosing is different.
• In combination, talquetamab is administered every 2 weeks, while teclistamab is given at a higher dose and less frequent interval (3 mg/kg every 2 weeks) compared with weekly dosing when used as monotherapy (1.5 mg/kg every week).</td></tr>
</table>

Combination	Epcoritamab-bysp (EPKINLY®) and R^2 (Lenalidomide and Rituximab) [25]	Teclistamab-cqyv (TECVAYLI®) and Talquetamab-tgvs (TALVEY®) [26, 27]
Additional Considerations	• REMS program with lenalidomide	• Both agents require unique REMS Dispense Authorizations (RDAs).
Any Grade Adverse Events (with >25% Incidence)	Rash (46%), upper respiratory tract infections (33%), fatigue (31%), injection site reactions (27%), constipation (26%)	CRS (79%), neutropenia (73%), taste changes (65%), nonrash skin adverse event (61%), anemia (56%), nail-related adverse event (52%), pyrexia (51%), diarrhea (48%), cough (45%), dry mouth (43%), thrombocytopenia (43%), COVID-19 (40%), rash adverse event (39%), pneumonia (36%), weight decrease (34%), fatigue (28%)
Grade 3 or > Adverse Events (with >25% Incidence)	None	Neutropenia (68%), anemia (38%), thrombocytopenia (30%)
Initial Approval	November 18, 2025	**Not** FDA-approved as of February 2, 2026
Pivotal Trial	EPCORE FL-1	RedirecTT-1

Table 4 (2 of 2). BTCEs in Combination Regimens

Combination	Epcoritamab-bysp (EPKINLY®) and GEMOX (Gemcitabine and Oxaliplatin) [28]		Glofitamab-gxbm (COLUMVI™) and GEMOX (Gemcitabine and Oxaliplatin) [29]		
Indication(s)	DLBCL following 1 or more lines of therapy		DLBCL following 1 or more lines of therapy		
Dosing Schedule	Cycle length: 28 d		Cycle length: 21 d		
	Epcoritamab	**GEMOX**	**Obinutuzumab**	**Glofitamab**	**GEMOX**
	C1-3: Day 1, 8, 15, and 22 C4-12: Day 1	C1-4: Gemcitabine: Day 1 and 15 Oxaliplatin: Day 1 and 15	C1D1 only	C1: Day 8 and Day 15 C2-12: Day 1	C1-8: Gemcitabine: Day 1 Oxaliplatin: Day 1
CRS Mitigation					
SUD Schedule	C1D1: 0.16 mg C1D8: 0.8 mg C1D15: 48 mg (FFD) C1D22: 48 mg		C1D1: Obinutuzumab C1D8: 2.5 mg (first dose of glofitamab) C1D15: 10 mg C2D1: 30 mg (FFD)		
Premedications	(1) Acetaminophen 650–1,000 mg (2) Diphenhydramine 50 mg (or equivalent) (3) Dexamethasone 15 mg or prednisolone 100 mg (or equivalent), before C1 treatments and for 3 consecutive days after Continue dexamethasone thereafter if G2 or G3 CRS with prior dose.		(1) Acetaminophen 500–1,000 mg (2) Diphenhydramine 50 mg (or equivalent) (3) Dexamethasone 20 mg (or equivalent) on C1D8, C1D15, C2D1, and C3D1. Continue dexamethasone thereafter if CRS occurs with prior dose.		
Hospitalization	C1D15 (FFD): 24-h admission		C1D8 (first glofitamab dose): 24-h admission		
CRS Incidence	**G1**	**G2**	**G3**	**G4-5**	**G1**	**G2**	**G3**	**G4-5**
	28%	23%	1%	0%	31%	11%	2%	0%
	Time course for CRS onset		**Median time to onset of CRS**		**Time course for CRS onset**		**Median time to onset of CRS**	
	C1: 84% C1D15 (FFD): 63%		Most events occurred in C1 following FFD.		C1D8: 35 C1D15: 13% C2D1: 11% C3D1: 7% C4+: 11%		C1D8: 14 h C1D15: 32 C2D1: 38 h C3+: 37 h	
ICANS Incidence	Any grade: 3% (G3: 1%)				Any grade: 2% (G3: 1%)			
What is Different Between the Single Agent(s) and Combination Therapy?	• Combination allows dose-dense GemOx without new safety signals.				• Glofitamab combination therapy retains the same obinutuzumab lead-in and step-up dosing strategy as monotherapy; differences are primarily related to the addition of fixed-duration chemotherapy rather than changes to glofitamab administration.			
Additional Considerations	• Fixed duration GemOx				• Fixed duration GemOx • A single dose of obinutuzumab is administered on C1D1, 7 days prior to the first glofitamab dose, for CRS mitigation.			
Any Grade Adverse Events (with >25% Incidence)	Thrombocytopenia (73%), infections (72%), neutropenia (65%), anemia (59%), CRS (52%), diarrhea (47%), nausea (40%), fatigue (35%), hypokalemia (31%), pyrexia (29%), COVID-19 (29%), increased ALT (28%), increased AST (25%), peripheral neuropathy (25%)				Thrombocytopenia (48%), CRS (44%), neutropenia (42%), anemia (41%), nausea (39%), peripheral neuropathy (36%), diarrhea (34%), increased AST (33%), increased ALT (32%)			

Combination	Epcoritamab-bysp (EPKINLY®) and GEMOX (Gemcitabine and Oxaliplatin) [28]	Glofitamab-gxbm (COLUMVI™) and GEMOX (Gemcitabine and Oxaliplatin) [29]
Grade 3 or > Adverse Events (with >25% Incidence)	Thrombocytopenia (59%), neutropenia (57%), anemia (43%), infections (29%)	Not reported
Initial Approval	**Not** FDA-approved as of February 2, 2026	**Not** FDA-approved as of February 2, 2026
Pivotal Trial	EPCORE NHL-2	STARGLO

Abbreviations: ALL: Acute Lymphoblastic Leukemia; ALP: alkaline phosphatase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BCMA: B-Cell Maturation Antigen; BCP: B-cell Precursor; BTCE: Bispecific T-Cell Engager; CR: Complete Response; CrCl: Creatinine Clearance; CRS: Cytokine Release Syndrome; C: Cycle; CD: Cluster of Differentiation; D: Day; DLBCL: Diffuse Large B Cell Lymphoma; DLL3: Delta-like ligand 3; ES-SCLC: Extensive Stage Small Cell Lung Cancer; FFD: First full dose; FL: Follicular Lymphoma; G1: Grade 1; G2: Grade 2; G3: Grade 3; G4: Grade 4; G5: Grade 5; GGT (gamma-glutamyl transferase), GPRC5D: G-protein-coupled receptor, class C, group 5, member D; HLA: Human Leukocyte Antigen; ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome; IQR: Interquartile Range; IV: Intravenous; LBCL: Large B-Cell Lymphoma; MM: Multiple Myeloma; MRD: Minimal Residual Disease; N/A: Not applicable; NS: Normal Saline; PTT: Partial Thromboplastin Time; PR: Partial Response; R/R: relapsed or refractory; SC: Subcutaneous; SD: Stable Disease; VGPR: Very Good Partial Response; WBC: White Blood Cell

Authors: Kelly M Brunk, PharmD, MBA, BCOP, and Madelyn Floysand, PharmD

REFERENCES

1. Mosunetuzumab (Lunsumio) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761263s005lbl.pdf

2. Mosunetuzumab (Lunsumio Velo) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2025. www.accessdata.fda.gov/drugsatfda_docs/label/2025/761263s006lbl.pdf

3. Budde LE, Sehn LH, Matasar M, et al. Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicentre, phase 2 study. *Lancet Oncol.* 2022;23(8):1055-1065. doi:10.1016/s1470-2045(22)00335-7.

4. Epcoritamab (Epkinly) [prescribing information]. Plainsboro, NJ: Genmab US, Inc. and North Chicago, IL: AbbVie Inc; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761324s009lbl.pdf

5. Thieblemont C, Phillips T, Ghesquieres H, et al. Epcoritamab, a novel, subcutaneous CD3xCD20 bispecific T-Cell–Engaging Antibody, in relapsed or refractory large B-Cell lymphoma: dose expansion in a phase I/II trial. *J Clin Oncol.* 2023;41(12):2238-2247. doi:10.1200/jco.22.01725.

6. Glofitamab (Columvi) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761309s004lbl.pdf

7. Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory diffuse large B-Cell lymphoma. *N Engl J Med.* 2022;387(24):2220-2231. doi:10.1056/nejmoa2206913.

8. Teclistamab (Tecvayli) [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761291s013lbl.pdf

9. Moreau P, Garfall AL, Van De Donk NWCJ, et al. Teclistamab in relapsed or refractory multiple myeloma. *N Engl J Med.* 2022;387(6):495-505. doi:10.1056/nejmoa2203478.

10. Talquetamab (Talvey) [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761342s016lbl.pdf

11. Chari A, Minnema MC, Berdeja JG, et al. Talquetamab, a T-ell–redirecting GPRC5D bispecific antibody for multiple myeloma. *N Engl J Med.* 2022;387(24):2232-2244. doi:10.1056/nejmoa2204591.

12. Elranatamab (Elrexfio) [prescribing information]. New York, NY: Pfizer Inc.; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761345s003lbl.pdf

13. Lesokhin AM, Tomasson MH, Arnulf B, et al. Elranatamab in relapsed or refractory multiple myeloma: phase 2 MagnetisMM-3 trial results. *Nat Med.* 2023;29(9):2259-2267. doi:10.1038/s41591-023-02528-9.

14. Linvoseltamab (Lynozyfic) [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals Inc; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761400s000lbl.pdf

15. Bumma N, Richter J, Jagannath S, et al. Linvoseltamab for treatment of relapsed/refractory multiple myeloma. *J Clin Oncol.* 2024;42(22):2702-2712. doi:10.1200/JCO.24.01008

16. Blinatumomab (Blincyto) [prescribing information]. Thousand Oaks, CA: Amgen Inc.; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125557s032lbl.pdf

17. Kantarjian H, Stein A, Gökbuget N, et al. Blinatumomab versus chemotherapy for advanced acute lymphoblastic leukemia. *N Engl J Med.* 2017;376(9):836-847. doi:10.1056/nejmoa1609783.

18. Gökbuget N, Dombret H, Bonifacio M, et al. Blinatumomab for minimal residual disease in adults with B-cell precursor acute lymphoblastic leukemia [published correction appears in Blood. 2019 Jun 13;133(24):2625. doi: 10.1182/blood.2019001109]. *Blood.* 2018;131(14):1522-1531. **doi:10.1182/**blood-2017-08-798322

19. Locatelli F, Zugmaier G, Rizzari C, et al. Effect of blinatumomab vs chemotherapy on event-free survival among children with high-risk first-relapse B-Cell acute lymphoblastic leukemia: a randomized clinical trial. *JAMA.* 2021;325(9):843-854. doi:10.1001/jama.2021.0987

20. Tebentafusp (Kimmtrak) [prescribing information]. Conshohocken, PA: Immunocore Commercial LLC; 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761228s003lbl.pdf

21. Hassel JC, Piperno-Neumann S, Rutkowski P, et al. Three-year overall survival with tebentafusp in metastatic uveal melanoma. *N Engl J Med.* 2023;389(24):2256-2266. doi:10.1056/nejmoa2304753.

22. Tarlatamab (Imdelltra) [prescribing information]. Thousand Oaks, CA: Amgen Inc.; 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761344s001lbl.pdf

23. Ahn MJ, Cho BC, Felip E, et al. Tarlatamab for patients with previously treated small-cell lung cancer. *N Engl J Med.* 2023;389(22):2063-2075. doi:10.1056/nejmoa2307980.

24. Mountzios G, Sun L, Cho BC, et al. Tarlatamab in small-cell lung cancer after platinum-based chemotherapy. *N Engl J Med.* 2025;393(4):349-361. doi:10.1056/NEJMoa2502099

25. Falchi L, Nijland M, Huang H, et al. Epcoritamab, lenalidomide, and rituximab versus lenalidomide and rituximab for relapsed or refractory follicular lymphoma (EPCORE FL-1): a global, open-label, randomised, phase 3 trial. *Lancet.* 2026;407(10524):161-173. doi:10.1016/S0140-6736(25)02360-8

26. Cohen YC, Magen H, Gatt M, et al. Talquetamab plus teclistamab in relapsed or refractory multiple myeloma. *N Engl J Med.* 2025;392(2):138-149. doi:10.1056/NEJMoa2406536

27. Kumar S, Mateos MV, Ye JC, et al. Dual targeting of extramedullary myeloma with talquetamab and teclistamab. *N Engl J Med.* 2026;394(1):51-61. doi:10.1056/NEJMoa2514752

28. Brody JD, Jørgensen J, Belada D, et al. Epcoritamab plus GemOx in transplant-ineligible relapsed/refractory DLBCL: results from the EPCORE NHL-2 trial. *Blood.* 2025;145(15):1621-1631. doi:10.1182/blood.2024026830

29. Abramson JS, Ku M, Hertzberg M, et al. Glofitamab plus gemcitabine and oxaliplatin (GemOx) versus rituximab-GemOx for relapsed or refractory diffuse large B-cell lymphoma (STARGLO): a global phase 3, randomised, open-label trial. *Lancet.* 2024;404:1940-1954. doi:10.1016/S0140-6736(24)01774-4