


Taking a BiTE Out of the CAR T-Cell Therapy Space

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Objectives

- Summarize CAR T-cell therapy and bispecific T-cell engager (BiTE) therapy literature and toxicities
- Compare logistical considerations pertaining to CAR T-cell therapies and BiTE therapies
- Review patient cases assessing the need for specific cellular therapy treatments




Lymphoma

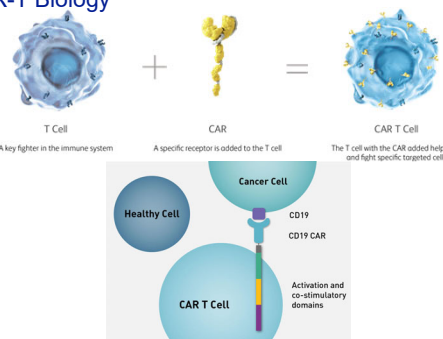
Axicabtagene ciloleucel (YESCART™)
 Brexucabtagene autoleucel (TECARTUS™)
 Tisagenlecleucel (KYMRIA™)
 Lisocabtagene maraleucel (BREYANZI®)

Multiple Myeloma


Idecabtagene vicleucel (ABECMA®)
 Ciltacabtagene autoleucel (CARVYKT™)



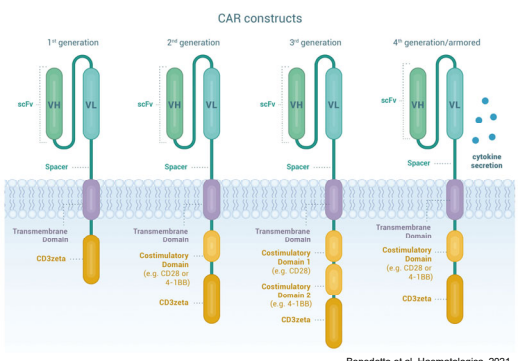
CAR-T Biology




T Cell: A key fighter in the immune system
 CAR: A specific receptor is added to the T cell
 CAR T Cell: The T cell with the CAR added helps find and fight specific targeted cells



CAR constructs




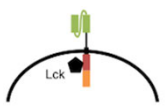
Benedetto et al, Haematologica, 2021



Product	Antigen-binding domain	Hinge region	Transmembrane region	Co-stimulatory domain	T cell activation domain	FDA approval (year)
Axicabtagene ciloleucel	Anti-CD19	CD28	CD28	CD28	CD3ζ	• LBCL refractory to first-line therapy or relapsing <12 months of first-line therapy (2022) • Relapsed LBCL after <2 lines of therapy (2017) • Relapsed FL after <2 lines of therapy (2021)
Brexucabtagene autoleucel	Anti-CD19	CD28	CD28	CD28	CD3ζ	• R/R MCL (2020) • R/R B-ALL (2021)
Tisagenlecleucel	Anti-CD19	CD28	CD28	4-1BB	CD3ζ	• LBCL after <2 lines of therapy (2018) • FL after <2 lines of therapy (2022)
Lisocabtagene maraleucel	Anti-CD19	IgG4	CD28	4-1BB	CD3ζ	• LBCL refractory to first-line or relapsing <12 months of first-line therapy or relapsing on first-line therapy and not eligible for HSCT (2022) • Relapsed LBCL after <2 lines of therapy (2021)
Idecabtagene vicleucel	Anti-BCMA	CD28	CD28	4-1BB	CD3ζ	Fifth line RRMM (2021)
Ciltacabtagene autoleucel	Dual anti-BCMA	CD28	CD28	4-1BB	CD3ζ	Fifth line RRMM (2022)

Cappelli, K.M., *Nat Rev Clin Oncol*, 2023

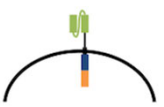




CD28/CD3z CART T cells

- Rapid and strong signaling
- Effector cell-like phenotype
- Exhaust in an in vivo model of disseminated lymphoma
- Intense signal generation

Axi-cel (Yescarta)
<6 weeks persistence



4-1BB/CD3z CART T cells

- Slow and weaker signaling
- Memory cell-like phenotype
- Resist exhaustion and prolong survival in an in vivo model of disseminated lymphoma

Tisa-cel (Kymriah)
Long term persistence >1-7 years

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Manufacturing and Infusion

Workup for CAR T-cell Eligibility

- Adequate renal, hepatic, cardiac, and pulmonary function
- No active infection
- No uncontrolled endocrine comorbidities
- Adequate performance status
- Insurance approval

CAR T-cell Therapy

Remove blood from patient to get T cells → Make CAR T cells in the lab (insert gene for CAR) → CAR T cells bind to cancer cells and kill them

Day 0 to Day 28: Post-infusion monitoring

Day -6 to Day -1: Lympho-depleting chemo

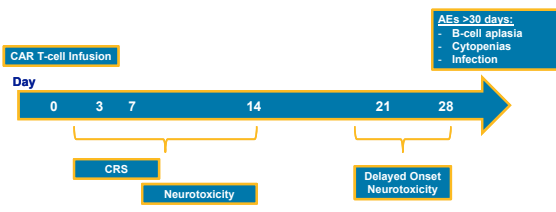
Estimated 3-6 weeks manufacturing time (variable)

Estimated 3-6 weeks manufacturing time (variable)

Variable per product commonly ~3 days of flutasteride + cyclophosphamide and ~2 days of rest prior to cell infusion

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General Toxicity Timeline



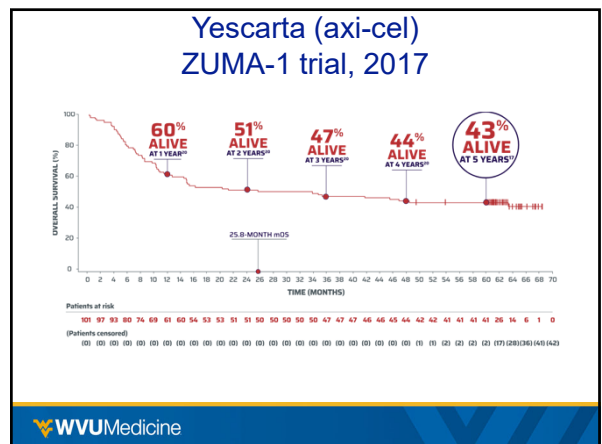
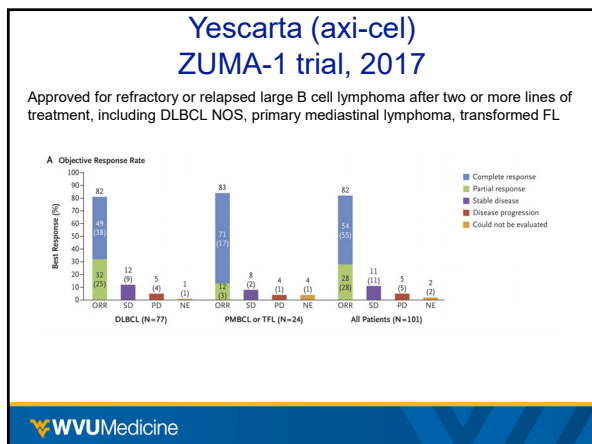
CRS (Days 0-14)
Neurotoxicity (Days 0-14)
Delayed Onset Neurotoxicity (Days 21-28)
AEs >30 days: B-cell aplasia, Cytopenias, Infection

**Patients instructed to avoid driving or operating heavy machinery for 8 weeks after cell infusion per REMS requirements*

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CAR T Cell Product Name and FDA Approval Date	Indication(s)	Target Antigen
Kymriah[®] (tisagenlecleomab) Approved by FDA in 2017	<ul style="list-style-type: none"> • Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or a second or later relapse. • Adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL), not otherwise specified (not otherwise specified) lymphoma, and DLBCL arising from follicular lymphoma. • Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy. 	CD19
Yescarta[®] (axicabtagene ciltecelomab) Approved by FDA in 2017	<ul style="list-style-type: none"> • Adult patients with large B-cell lymphoma that is refractory to first-line chemotherapy or that relapses within 12 months of first-line chemotherapy. • Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL), not otherwise specified, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 1B. • Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy. 	CD19
Yescarta[®] (axicabtagene ciltecelomab) Approved by FDA in 2020	<ul style="list-style-type: none"> • Adult patients with relapsed or refractory mantle cell lymphoma (MCL). • Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). 	CD19
Breyanzi[®] (lisinacabtagene mauecelomab) Approved by FDA in 2021	<ul style="list-style-type: none"> • Adult patients with large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL), not otherwise specified (including DLBCL arising from mediastinal lymphoma, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B), who have: • relapsed disease to first-line chemotherapy or relapse within 12 months of first-line chemotherapy; or • relapsed disease to first-line chemotherapy or relapse after first-line chemotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidity or age; or • relapsed or refractory disease after two or more lines of systemic therapy. 	CD19
Abraxa[®] (idecabtagene vixtaceleomab) Approved by FDA in 2021	Adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.	BCMA
Carysata[®] (ciltacabtagene autemecelomab) Approved by FDA in 2022	Adult patients with relapsed or refractory multiple myeloma after two or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.	BCMA

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Yescarta (axi-cel) ZUMA-7 trial, 2022

Approved for refractory or relapsed within 12 months large B cell lymphoma

R/R LBCL (N=359)

Key eligibility:

- Aged ≤ 18 years
- LBCL
- R/R ≤ 12 months of 1L therapy*
- Intended to proceed to HD1+ASCT

Stratification:

- Response to 1L therapy
- Second-line age-adjusted IP†

Randomized 1:1

YESCARTA (N=180)

Lymphodepleting chemotherapy + YESCARTA*

Standard therapy (N=179)

2-3 cycles of investigator-selected platinum-based chemoimmunotherapy*

Initial disease assessment (day 50)

Responders (CR or PR)
HD1+ASCT

Nonresponders
Additional treatment off protocol†

Day 100 assessment
Day 150 assessment
Long-term follow-up assessment

Yescarta (axi-cel) ZUMA-7 trial, 2022

Approved for refractory or relapsed within 12 months large B cell lymphoma

Overall Survival

Median Overall Survival (95% CI):
 Yescarta: 15.7 (14.1-17.3)
 Standard Care: 11.9 (10.3-13.5)
 P < .001

Progression-Free Survival

Median Progression-Free Survival (95% CI):
 Yescarta: 14.7 (13.1-16.3)
 Standard Care: 10.2 (8.6-11.8)
 P < .001

ZUMA-7. NEJM, 2022

Tecartus (brexu-cel) ZUMA-2 trial, 2020

Approved for relapsed or refractory mantle cell lymphoma, adults with refractory or relapsed B-cell ALL

A. Best Response

Number of Patients

Objective Response: 14 (37%)
 Stable Disease: 2 (5%)
 Progressive Disease: 2 (5%)

Complete response: 14 (37%)
 Partial response: 2 (5%)

B. Duration of Response

Percent of Patients with Response

Median, not reached (95% CI, 8.6-NE)

C. Progression-Free Survival

Percent of Patients

Median, not reached (95% CI, 9.2-NE)

D. Overall Survival

Percent of Patients Alive

Median, not reached (95% CI, 24.0-NE)

ZUMA-2 trial, NEJM 2020

Kymriah (tisa-cel) JULIET trial, 2018

Approved for refractory or relapsed large B cell lymphoma after two or more lines of treatment.
 Approved for refractory B cell ALL up to 25 yo or after second relapse.
 Also approved for FL after 2 lines of treatment (ELARA trial).

A. Duration of Response

Percent of Patients with Response

Median, not reached (95% CI, 11.1-NE)

B. Progression-Free Survival

Percent of Patients

Median, not reached (95% CI, 11.1-NE)

C. Overall Survival

Percent of Patients Alive

Median, not reached (95% CI, 11.1-NE)

D. Overall Survival

Percent of Patients Alive

Median, not reached (95% CI, 11.1-NE)

JULIET. NEJM, 2019

Breyanzi (liso-cel) TRANSFORM trial, 2021

Approved for refractory or relapsed large B cell lymphoma after two or more lines of treatment, including DLBCL NOS, primary mediastinal lymphoma, transformed FL.
 Approved for refractory or relapsed within 12 months large B cell lymphoma.

Breyanzi mEFS: NR, 95% CI (8.5, NR)
 Standard therapy mEFS: 2.4 months, 95% CI (2.2, 4.8)

FDA approved CAR T-cell therapies

KYMRIAH

2017

YESCARTA

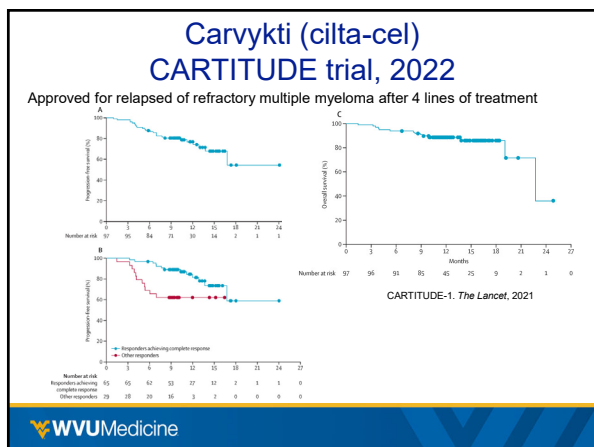
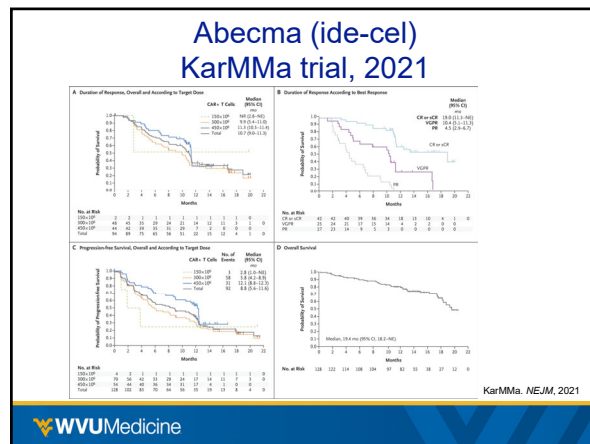
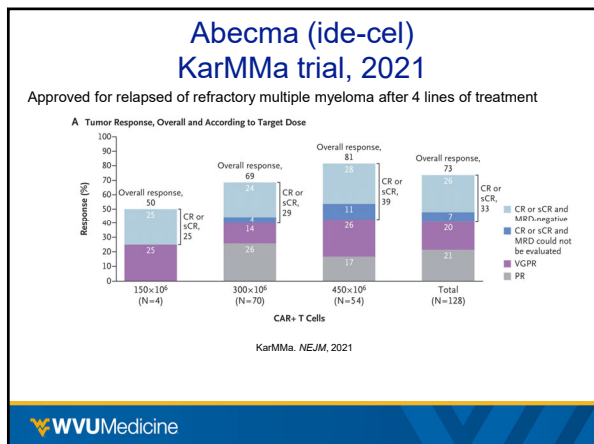
2017

TECARTUS

2020

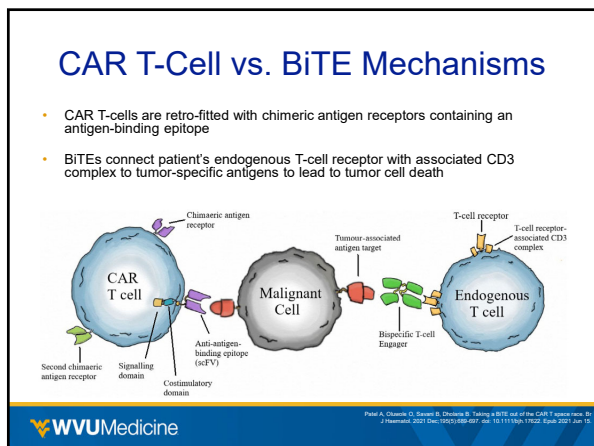
Breyanzi

2021



CAR T-Cell Therapy Logistics

- Finite treatment duration is great for some patients – “one and done” for now
- Social determinants of health may restrict some patients from receiving CAR T-cell therapy
- Manufacturing – possible delays (may not be great for those rapidly progressing)
- Possible needing for bridging chemo (may not be great for frail patients)
- Need for lymphodepleting chemotherapy
- Administration – recommended inpatient though many centers follow outpatient protocols



Paving the Way

Trial and Regimen	Patient Population	Dose	Results	FDA Approval
TOWER Phase 3 Blenatumomab vs. standard-of-care (SOC) chemotherapy	405 patients with R/R B-cell ALL	<u>Continuous infusion</u> Cycle 1: 9 mcg/day on days 1-7 28 mcg/day on days 8-28 of 42-day cycle Cycles 2-5: 28 mcg/day on days 1-28 of 42-day cycles Cycles 6-9: 28 mcg/day on days 1-28 of 84-day cycle	Median overall survival (OS): 7.7 months vs. 4.6 months (P<0.01) Complete remission (CR) with full hematologic recovery: 34% vs. 16% (P<0.001) Longer median duration of remission: 7.3 vs. 4.6 months Adverse events ≥grade 3: 87% vs. 92%	First BiTE approved December 3, 2014
GO29781 Phase 2 Mosunetuzumab-arg	90 R/R follicular lymphoma patients ≥1p-2 lines of therapy, including anti-CD20 and alkylating agents	<u>Intravenous</u> Step-up dosing C1D1: 1 mg C1D6: 2 mg C1D15: 60 mg C2D1: 60 mg C3 and beyond: 30 mg	Objective response rate: 80% CR: 60% Median duration of response: 22.8 months Most common grade 3-4 adverse events: neutropenia, hypophosphatemia, hyperglycemia, and anemia	December 22, 2022


WVU Medicine

Lymphoma

Epcoritamab-bysp (Epkinyl™)
Glofitamab-gxbm (Columvi™)


Multiple Myeloma

Teclistamab-cqyv (Tecvayli®)
Talquetamab-tgvs (Talvey™)
Elranatamab-bcmm (Elrexio™)



Additional BiTE Therapy Approvals

Approval Date	Agent	Target	Indication	Trial
October 25, 2022	Teclistamab-cqyv (Tecvayli®)	BCMA	R/R multiple myeloma (MM) having received > 4 prior lines of therapy, including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD), and an anti-CD38 monoclonal antibody	MajesTEC-1
May 19, 2023	Epcoritamab-bysp (Epkinyl™)	CD20	R/R diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma (HGBL) after ≥ 2 lines of systemic therapy	EPCORE NHL-1
June 15, 2023	Glofitamab-gxbm (Columvi™)	CD20	R/R DLBCL-NOS or large B-cell lymphoma arising from follicular lymphoma (FL) after ≥ 2 lines of systemic therapy	NP30179
August 9, 2023	Talquetamab-tgvs (Talvey™)	GPRCSD	R/R MM having received > 4 prior lines of therapy, including a PI, IMiD, and an anti-CD38 monoclonal antibody	MMY1001 (MonumentAL-1)
August 14, 2023	Elranatamab-bcmm (Elrexio™)	BCMA	R/R MM having received > 4 prior lines of therapy, including a PI, IMiD, and an anti-CD38 monoclonal antibody	MagnetisMM-3




Center for Drug Evaluation and Research, Oncology (cancer) / hematologic malignancies approval notifications. U.S. Food and Drug Administration. <https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-center-hematologic-malignancies-approval-notifications>

Teclistamab-cqyv (Tecvayli®)


MajesTEC-1	
Objective	Assess the efficacy and safety of teclistamab in patients with RR MM
Methods	Phase 1-2 study in RRMM after ≥3 lines of therapy including triple-class exposure to IMiD, PI, and anti-CD38 antibody
Patients	N=165 • Median age: 64 years (33-84) • Median number of prior lines of therapy: 5 • 77.6% triple-class refractory • 28% high-risk cytogenetics • 17% extramedullary disease
Outcomes	Primary: overall response rate (ORR) (partial response or better)

Subcutaneous administration



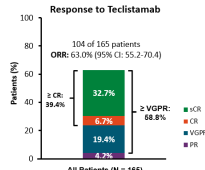
once weekly dosing (1.5 mg/kg)

Until disease progression or unacceptable toxicity



MajesTEC-1: Results

Response to Teclistamab




104 of 165 patients
ORR: 63.0% (95% CI: 55.2-70.4)

All Patients (N = 165)

Outcomes	Patients (N=165)
MRD negativity at 10 ⁻⁵ , n (%)	44 (26.7)
Median DoR, mo	18.4
Median PFS, mo	11.3
Median OS, mo	18.3
TTR, mo	First: 1.2 months Best: 3.8 months

Safety	
Neutropenia, 70.9%	CRS, 72.1% (grade 3/4, 0.6%)
Anemia, 52.1%	Neurotoxic event, 14.5% (grade 3/4, 0.6%)
Thrombocytopenia, 40%	Infections, 76.4%



Talquetamab-tgvs (Talvey™)


MonumentAL-1	
Objective	Assess the efficacy and safety of talquetamab in patients with RR MM
Methods	Phase 1-2 study in RRMM after ≥3 lines of therapy including triple-class exposure to IMiD, PI, and anti-CD38 antibody
Patients	N=130 • Median age: 64 years (34-84) • Median number of prior lines of therapy: 6 • 75% triple-class refractory • 16% high-risk cytogenetics • 32% extramedullary disease
Outcomes	Primary: frequency and type of dose-limiting toxic effects (study part 1 only)

Subcutaneous administration

TALVEY® WEEKLY DOSING SCHEDULE			
Dosing schedule	Day	Step-up dose ^a	Dose ^b
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4 ^c	Step-up dose 2	0.06 mg/kg
	Day 7 ^c	First treatment dose	0.4 mg/kg
Weekly dosing schedule	One week after first treatment dose and weekly thereafter ^d	Subsequent treatment doses	0.4 mg/kg once weekly

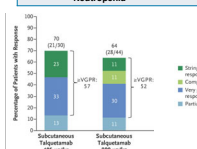
OR

TALVEY® BIWEEKLY (EVERY 2 WEEKS) DOSING SCHEDULE			
Dosing schedule	Day	Step-up dose ^a	Dose ^b
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4 ^c	Step-up dose 2	0.06 mg/kg
	Day 7 ^c	Step-up dose 3	0.4 mg/kg
Biweekly (every 2 weeks) dosing schedule	Day 10 ^d	First treatment dose	0.8 mg/kg
	Day 24 ^d	Subsequent treatment doses	0.8 mg/kg every 2 weeks




MonumentAL-1 Results

Safety		
Common Adverse Events	Weekly Dosing (n=30)	Biweekly Dosing (n=44)
CRS	77% 3%	80% 0%
Neurotoxicity	10% 0%	5% 0%
Skin-related events	67% 0%	70% 2%
Nail-related events	57% 0%	27% 2%
Dysgeusia	63% N/A	57% N/A
Neutropenia	67% 60%	36% 32%



Outcomes	Patients (N=74)
Median DoR, mo	Weekly: 10.2 Biweekly: 7.8
Median TTR, mo	Weekly: 0.9 Biweekly: 1.2



Elranatamab-bcmm (Elrexio™)

MagnetisMM-3

Objective Assess the efficacy and safety of elranatamab in patients with R/R MM

Methods Phase 2 study in RRMM after ≥3 lines of therapy including triple-class refractory to IMiD, PI, and anti-CD38 antibody

Patients N=123
 • Median age: 68 years (36-89)
 • Median number of prior lines of therapy: 5
 • 96.7% triple-class refractory
 • 25.2% high-risk cytogenetics
 • 31.7% extramedullary disease

Outcomes Primary: ORR

Subcutaneous administration

2 step-up doses 1st treatment dose

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MagnetisMM-3 Results

Outcomes	
MRD negativity at 10⁻⁴, n (%)	23 (92)
Median DoR	Not reached (71.5% probability of maintaining response at 15 months)
Median PFS and OS	Not reached at 12 months
PFS Rate	57.1% at 12 months
OS Rate	62% at 12 months
TTR	1.7 months

Safety (n=123), Any Grade	
Neutropenia, 60 (48.8)	Thrombocytopenia, 38 (30.9)
Anemia, 60 (48.8)	Injection site reaction, 33 (26.8)

Safety (n=119)	
CRS	ICANS
67 (56.3)	4 (3.4)
Time to Onset, 2 days	Time to Onset, 2.5 days

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Epcoritamab-bysp (Epkiny™)

EPCORE NHL-1

Objective Assess the efficacy and safety of epcoritamab in patients with R/R DLBCL, NOS, including DLBCL arising from indolent lymphoma, and HGCL

Methods Phase 1-2 study in patients with LBCL ≥ 2 lines of systemic therapy including at least one anti-CD20 monoclonal antibody-containing therapy

Patients N=157
 • Median age: 65 years (22-83)
 • Median number of prior lines of therapy: 3
 • 60% primary refractory
 • 18% prior autologous stem cell transplant
 • 39% prior CAR-T-cell therapy

Outcomes Primary: ORR

Subcutaneous administration

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EPCORE NHL-1 Results

Outcomes (n=148)	
MRD negativity at 10⁻⁴, n (%)	52/112 (46.4)
Median DoR (CR)	20.8 months
Median PFS	Not reached
Median OS	18.5 months
TTR	2.7 months

Safety, Any Grade	
Neutropenia, 24%	Fatigue, 23%
Pyrexia, 24%	Nausea, 22%
Diarrhea, 21%	CRS, 51% (grade 3, 3%)

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Glofitamab-gxbm (Columvi™)

NP30179

Objective Assess the efficacy and safety of glofitamab in patients with R/R DLBCL, NOS, transformed FL, HGCL, or primary mediastinal large B-cell lymphoma

Methods Phase 2 study in patients with LBCL ≥ 2 lines of systemic therapy including at least one anti-CD20 monoclonal antibody-containing therapy and one anthracycline-containing regimen

Patients N=155
 • Median age: 66 years (21-90)
 • Median number of prior lines of therapy: 3
 • 58% primary refractory
 • 30% prior CAR-T-cell therapy

Outcomes Primary: CR

Intravenous administration

~8.5-month fixed-duration therapy

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NP30179 Results

Outcomes (n=155)		
Median DoR	18.4 months	
Median PFS	4.9 months	
Median OS	11.5 months*	
TTR	42 days	






Safety, Any Grade (n=154)	
Neutropenia, 38%	Fatigue, 23%
Anemia, 31%	Thrombocytopenia, 25%

Safety Continued		
Event	CRS	Neurologic
Occurrence	63%* (≥ grade 3, 4%)	8% (≥ grade 3, 3%)
Onset	13.5 hours*	N/A

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BiTE Therapy Logistics

Available off-the-shelf
 Ready-to-use, single-dose vials
 Rapid subcutaneous administration for most products
 Extended dosing intervals for most products
 Fixed dose options available
 Inpatient versus outpatient administration

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BiTE Therapy Costs

- Overall cost of a CAR T-cell therapies can potentially reach \$450,000
 - Depending on presence/severity of adverse effects, inpatient vs. outpatient administration, nursing/infusion center costs, pharmaceutical company
- \$2,554.74 per vial of glofitamab
 - \$30,656.88 for 12 cycles
- What about continuous duration administration?

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BiTE Therapy Costs

- Elranatamab's total Wholesale Acquisition Cost (WAC):

		Months 1-6	Months 7-12
	One 75 mg/1.9 mL (40 mg/mL) single-dose vial in a carton		One 44 mg/1.1 mL (40 mg/mL) single-dose vial in a carton
NDC	0069-4464-02	0069-2922-02	
WAC	\$13,050.72 per 1.9 mL vial	\$7,555.68 per 1.1 mL vial	

Average total cost of treatment for Year 1: ~\$41.5K / month

- Pfizer will provide elranatamab-bcmm 44 mg vials free of charge to support inpatient administration and monitoring for first two step-up doses

Program Enrollment

→

1st Order of Free Product

→

Free Product Shipment

→

Free Product Dispensation & Administration

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Sequencing

Agent	Trial	Results
Teclistamab	MajesTEC-1, cohort C	40 patients with prior BCMA-directed therapies - 52.5% ORR - 15 prior CAR T patients → 53.3% ORR
Talquetamab	MonumentAL-1	16 patients with prior BCMA-directed therapies - 50% ORR
Elranatamab	MagnetisMM-3, cohort B	87 patients with prior BCMA-directed therapies - 46% ORR - 36 prior CAR T patients → 52.8% ORR
Epcoritamab	EPCORE NHL-1	61 patients with prior CAR T-cell therapy - 54.1% ORR, 34.4% CR rate, 9.7 months mDOR
Glofitamab	NP30179	51 patients with prior CAR T-cell therapy - 35% CR

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Patient Cases

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63 Male with Multiple Myeloma

- Presented with rib pain and renal failure (creatinine of 4.35)
- Work up showed concern for multiple myeloma
 - Lambda light chain 9996.9
 - Durie-Salmon Stage IIIb
- Underwent bone marrow biopsy confirming multiple myeloma with 24% plasma cells and multiple areas of bone involvement on skeletal survey
- Initially started on Velcade (Bortezomib) and Dexamethasone and later had improved kidney function so added on Cytosan (Cyclophosphamide)
- Completed 4 cycles of Cyclophosphamide + Bortezomib + Dexamethasone then referred for autologous hematopoietic transplant

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63 Male with Multiple Myeloma (continued)

- Post-treatment bone marrow biopsy showed no morphologic or immunophenotypic evidence of residual plasma cell myeloma
 - FISH showed residual complex cytogenetics
- Underwent conditioning with melphalan and received autologous hematopoietic transplant
- Post-transplant course uncomplicated and was started on Revlimid (Lenalidomide), Velcade (Bortezomib) and Dexamethasone for maintenance therapy
 - Developed generalized blisters and purplish rash thought to be from Revlimid
 - Changed therapy to Pomalyst (Pomalidomide) + Velcade + Dexamethasone for 2 weeks, but had to discontinue Pomalidomide due to increasing creatinine.
 - Continued on Velcade + Dexamethasone
- No evidence of progression for 1 year after his autologous transplant and continued to follow with local oncologist



63 Male with Multiple Myeloma (continued)

- 1 year and 2 months after his transplant, lambda light chain levels started to rise
- Local oncologist started patient on Daratumumab + Pomalidomide + Dexamethasone for relapsed/refractory disease, but still continued to see progression based on light chain levels
- Switched to Carfilzomib + Xpovio (Selinexor), but continued to see progression in 6/2020
- Started on Cyclophosphamide + Bortezomib + Dexamethasone, but continue to see progression of disease
- Switched treatment to Blenrep (Belantamab) which showed response, but had patient experienced decreased visual acuity few months after initiation
- Started on Elotuzumab + Pomalidomide + Dexamethasone with evidence of progression of disease, rapid increase in light chains and worsening creatinine




What would you do?

Chimeric antigen receptor T-cell (CAR-T) therapy


Or

Bispecific T-cell engager (BiTE) therapy




60 Male with Diffuse Large B-cell Lymphoma

- Initially underwent cholecystectomy for cholecystitis but persisted to have pain for few months
- CT abdomen showed hepatic and pulmonary lesions and surrounding lymphadenopathy
- PET-CT showed activity in the liver, lungs, and lymph nodes
- Hepatic lesion biopsy showed diffuse large B-cell lymphoma
- Underwent treatment with Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) for 6 cycles



60 Male with Diffuse Large B-cell Lymphoma (continued)

- Referred for salvage therapy and autologous hematopoietic transplant evaluation
- Patient received 2 cycles of Rituximab, Ifosfamide, Carboplatin, Etoposide (R-ICE) with partial response
- Plan for autologous hematopoietic transplant
- Collection was unsuccessful despite best attempt for stem cell mobilization with Plerixafor




What would you do?

Chimeric antigen receptor T-cell (CAR-T) therapy

Or

Bispecific T-cell engager (BiTE) therapy




Conclusions

Favours BiTEs



<p>Advantages</p> <ul style="list-style-type: none"> • Off the shelf – immediate use • Scalability & access • Favorable toxicity profile • Use in treatment naïve patients (that, elderly) • Favorable cost profile in the short run • If cell expires, resolves with discontinuation of therapy <p>Disadvantages</p> <ul style="list-style-type: none"> • Complex antibody constructs • Dependent on endogenous T-cell function • Clinical duration of therapy • Durability of long term remissions unclear • Chronic administration leading to long term financial burden • Possible need for consolidative hematopoietic cell transplant to maintain long term remission 	<p>Disadvantages</p> <ul style="list-style-type: none"> • Ex vivo T-cell modification required • Production time required, delays or processing failures possible • Uplifted start to cost and administrative burden of CAR T • Institutional certification and specialization • Toxicity from CD3/CD28 and lymphodepleting chemotherapy • Concern for sequential malignancies <p>Advantages</p> <ul style="list-style-type: none"> • Uplifted financial toxicity • If cell expires and expenses of unpredictable duration <p>Advantages</p> <ul style="list-style-type: none"> • Finite duration of treatment • More prospective data available • Long term cure and remissions without additional treatment • Innovation for allogeneic CARs, CARs with multiple targets
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Favours CAR T

Papan A, Chavira G, Saveri B, Chandra B. Taking a BiTE out of the CAR T space. *Ann Hematol*. 2021 Dec;100(12):2548-2557. doi: 10.1016/j.ahem.2021.06.015.



Questions?

Taking a BiTE Out of the CAR T-Cell Therapy Space

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