Controversies in Cancer Care: Evidence, Interpretation, & Clinical Decision Making

CART-T vs Bispecific Antibodies in Earlier Lines of Therapy

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Disclosures

I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:
The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:
Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

Chimeric Antigen Receptor T –cell Products -Lymphoma

Product	Indication	Relapse< 1 yr.	Relapse>1 yr
Axi-cell (Yescarta)	LBCL/FL	Indicated	Need 2 or more lines of Rx
Liso-cell (Breyanzi)	LBCL/FL/CLL/ MCL	Indicated	Same as above CLL (BTK&BCL-2) MCL 2 or more +BTK
Brexu-cell (Tecartus)	MCL/ALL	Indicated	relapsed
Tisa-cell (Kymriah)	LBCL/FL/ALL	Indicated	Need 2 or more lines for LBCL % FL

Chimeric Antigen Receptor T-Cell Products Myeloma

Product	indication
Ide-Cell (Abecma)	Relapsed/refractory to Anti-CD38 & proteosome inhibitor
Cilta-Cell (Carvykti)	Same as above

Bispecific T-cell Engagers (BITES) Myeloma & Lymphoma FDA approved

Product	Indication	Engagement	Prior Therapy
epcoritamab	R/R LBCL/FL	CD20 & CD3	Two or more lines of prior therapy
glofitamab	R/R LBCL	CD20 & CD3	Two or more lines of prior therapy
mosunetuzumab	R/R FL	CD20 & CD3	Two or more lines of prior therapy
teclistamab	R/R Myeloma	BCMA & CD3	Four or more lines of prior therapy (imide, protesome, Anti-CD38)
talquetamab	R/R Myeloma	GPRC5D & CD3	Four or more lines of prior therapy Same as above

Pro & Cons of Bispecifics vs CAR Tcell

Bispecifics

PROS:

Off the shelf

No Manufacturing process

Easy to administer (ambulatory)

Fewer adverse effects

CONS:

Multiple doses

Lower CR rate

Duration of PFS less

Curative ??

CAR T

PROS:

Single Dose

Robust CR rate

Longer duration of PFS

10 yr PFS suggests that they are curative

CONS:

Ability to collect adequate no. of lymphocytes

Manufacturing process

Bridging therapy

Higher rate of adverse effects

Hospital stay

The race is on : Bispecifics vs CAR-Tcells in B cell Lymphoma

Gurumurthi et al. Blood Advances (2023)7: 5712.

	Zuma 1 Axi-cell	Juliet Tisa-cell	Transcend Liso-cell	epcoritamab	glofitamab
CR %	58	40	53	39	39
1 yr. PFS %	44	na	49	na	37
CRS (grade 3) %	13	22	2	2.5	4
iCANS (grade 3) %	23	12	10	0.6	3

CAR-T cell vs Bispecific Antibody as Third or Later line in Large B-cell Lymphoma Therapy: a meta-analysis.

Kim et al. Blood(2024)144:629

Performed a literature search (Medline, Combase, and Cochrane)

Identified 16 studies involving 1347 patients

CR rate:	CAR T 51%	BITES 36%	
I year PFS	32%	14%	(p<0.01)
Grade 3 CRS	8%	1%	
Grade 3 iCANS	12%	1%	

Comparative Analysis of Bispecific Antibodies and CAR Tcell Therapy in Follicular Lymphoma (R/R)

Morabito et al. European J. Hematology.(2025)114:4

Trial	Product	CR %	Median PFS yrs
Zuma-5	Axi-cell	79	> 3 years
Transcend	Liso-cell	94	NYR
GO29781	mosunetuzumab	62	na

Ten-Year Outcome after CAR T-cell Therapy for B cell Lymphoma

Ruella et al NEJM(2026)394:2440

10-year follow up of 34 patients treated with Tisa-cell (24 pts LCL & 14 pts FL)

10-year PFS for LCL pts was 17% (4/24 pts) and 29% for FL pts (4/14)

Overall Survival was 17% and 50% respectively

Cautionary Notes:

9/38 patients (21%) developed second malignancies at 10 years including AML (3 pts), prostate cancer (2 pts), lung cancer (2 patients both smokers), mycosis fungoides (1 pt).

Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma

Munshi et al. NEJM(2021)384:705

Phase II involving 140 pts with prior therapy of an imide, protease inhibitor, and anti-CD38 monoclonal

Of these 140 pts, 128 evaluable

CR rate 42/128 (33%)

MRD rate (less than 10 to the -5th) 33/128 (26%)

Median PFS 8.8 months

CRS Grade 3 7/128 (5%)

iCANS Grade 3 0%

Long term remission and survival in patients with relapsed or refractory multiple myeloma treated with LCAR-B38 CAR T cells: 5 year follow up of the Legend -2 Trial.

Xu et al Journal of Hematology & Oncology (2024)17:22

74 pts with a median follow up of 65.4 months

5-year PFS 21%

5-year OS 28.4%

CR patients the 5-year PFS and OS were 28.4% and 65.7% respectively

Second malignancy rate 5.4%

Comparative efficacy and safety of BCMA targeted CAR T cell and BITES in refractory/relapsed myeloma: a meta-analysis of international and real-world studies.

Techaapornkun et al. Annals of Hematology (2025)104:4791

21 Studies involving 2246 patients analysis on 1357 pts (952 CAR T), (405 BITES)

	BITES	CAR T
Number of Patients	405	952
CR/stringent CR	166/405 (41%)	552/952 (58%)
MRD negative	131/166 (79%)	403/552 (73%)
Grade 3 CRS	1%	16%
Grade 3 iCANS	2%	6%
Infections	25%	15%

Teclistamab in Multiple Myeloma with *one to three* previous lines of therapy.

Touzeau et al. NEJM(2026)343:490

Randomized study involving 593 pts 34% were previously treated with 3 lines of prior therapy

296 received teclistamab and 297 PVD or KD

	Teclistamab	**PvD/KD**
No. CR stringent	159/296 (54.7%)	28/297 (9.4%)
18-month PSF	69.8%	29.6% (p<0.001)
18-month Survival	79.2%	68.6% (p=0.002)
Grade 3 CRS	2/296	
Grade 3 iCANS	0	
Pneumonia	44/297	30/297

Talquetamab-Daratumumab Relapsed or Refractory Myeloma

Mina et al. NEJM(2026)345:671

Randomized study 1-3 lines of prior therapy arms: Tal+DP, Tal+D, DPd

	TalDP (287)	TalD (287)	DPd (290)
CR %	71.1	69.0	34.5
PSF 2 yr %	81.3	77.6	51.2
OS 2 yr %	89.2	87.9	79
MRD 10 to -5	52.3%	46.3%	15.9%
CRS grade 3	0	0	
iCANS grade 3	2.9%	1.5%	

Lets focus on MRD

MRD is a valid endpoint in Multiple Myeloma
Landgren et al. Plenary Paper Blood 144:359 [2024]
(i.e. iberdomide)

- Multiple myeloma studies numbing 4907 patients
- The regression analysis correlated MRD negative status and PFS were 0.67 at the conclusion of therapy and 0.84 at 12 months
- "MRD maybe an early clinical end point to predict clinical benefit in multiple myeloma.....and may expedite the development of new drugs
- The FDA voted to approve MRD as clinically useful endpoint in evaluating myeloma clinical trials

Measurable Residual Disease Monitoring Lymphoma

Cuzzo et al Current Hematologic Malignancy Reports(2023)18:292

ClonoSEQ is FDA approved for monitoring MRD in DLBCL and CLL

NGS helps identify IgHVDJ rearrangements or translocations

MRD in CAR T using axi-cell has predictive value in detecting early relapse & shorter PFS

Early studies demonstrate predictive value in FL

If MRD is the ultimate endpoint in myeloma, surely the same will hold true in lymphoma

How do we achieve an MRD of less than 10^{-6} in DLBCL

ALPHA2 Study:Allo-501A Allogeneic CAR T in LBCL, Updated Results Continue to Show Encouraging Safety and Efficacy with Consolidation Dosing. Lekakis et al. Blood(2021)138 Supplement 1: 649-650

ALLO-501A is a of the shelf CAR T-cell that is genetically modified anti-CD19 that has been gene edited to disrupt the T-cell receptor constant gene and the CD52 gene to minimize the risk of GVHD and permit the use of an anti CD52 monoclonal antibody for selective lymphodepletion.

Single arm phase 1-2 trial in pts with R/RDLBCL, transformed FL, transformed MZL,& FL Grade 3B

20 pts enrolled, 15 evaluable heavily pretreated, median prior Rx 3 (3-7)

No CRS, No GVHD, no iCANS, cytopenias were universal and most common SAE

CR rate was 50%

4/15 patients received “consolidation” two successive doses of ALLO-501A and all achieved a CR

How do we achieve an MRD of less than 10^{-6} in DLBCL (continued)

ALPHA2 Study:Allo-501A Allogeneic CAR T in DLBCL treated with standard therapy but who fail to achieve MRD

Schema eligible pts DLCBL (ABC, germinal center B, double hit, triple hit, PMBCL) treated with standard therapy and achieve a CR by conventional imaging BUT are MRD positive:

RANDOMIZATION to: Allo-501A CAR T or observation (in patients who achieve a CR, surveillance is the standard approach)

Endpoints: PFS, time to relapse, conversion to MRD “negative” state

Q. Should CART-T & Bispecific Antibodies be Used in Earlier Lines of Therapy ?

A. Resounding YES

Ongoing Studies:

P1214 Subcutaneous Epcoritamab and RCHOP for first-line treatment of patients with high-risk diffuse large B cell lymphoma

COALITION Glofitamab plus RCHOP or polatuzumab-RCHP in patients with high-risk diffuse large B cell lymphoma

COH A phase ll study of epcoritamab and RGemOX as salvage/bridging therapy prior to autologous HSCT or CAR T

Allo-501A randomized study