

Oncology Pulse

Bluestar
BioAdvisors 

Challengers to Auto CAR-T in Liquid Tumors

November 2023

Bluestar
BioAdvisors 
























Challengers to Auto CAR-T in Liquid Tumors

Summary

- The approval of autologous chimeric antigen receptor (CAR)-T cell therapy dramatically improved outcomes for patients with multiple myeloma and aggressive lymphoma; however, the treatment comes with major logistical challenges, safety concerns and high cost
- More recently, bispecific T-cell engagers have emerged, offering an off-the-shelf alternative with potentially better safety but lower efficacy
- For now, autologous CAR-T is prioritized for those who are candidates for both, due to longer term data, especially as it relates to durability of response
- But, both approaches are seeking to push into earlier lines as part of combination regimens, and allogeneic CAR-Ts are aiming to provide the efficacy of CAR-T with an off-the-shelf product

There are two distinct T-cell therapy based approaches available to treat multiple myeloma (MM) and aggressive lymphomas

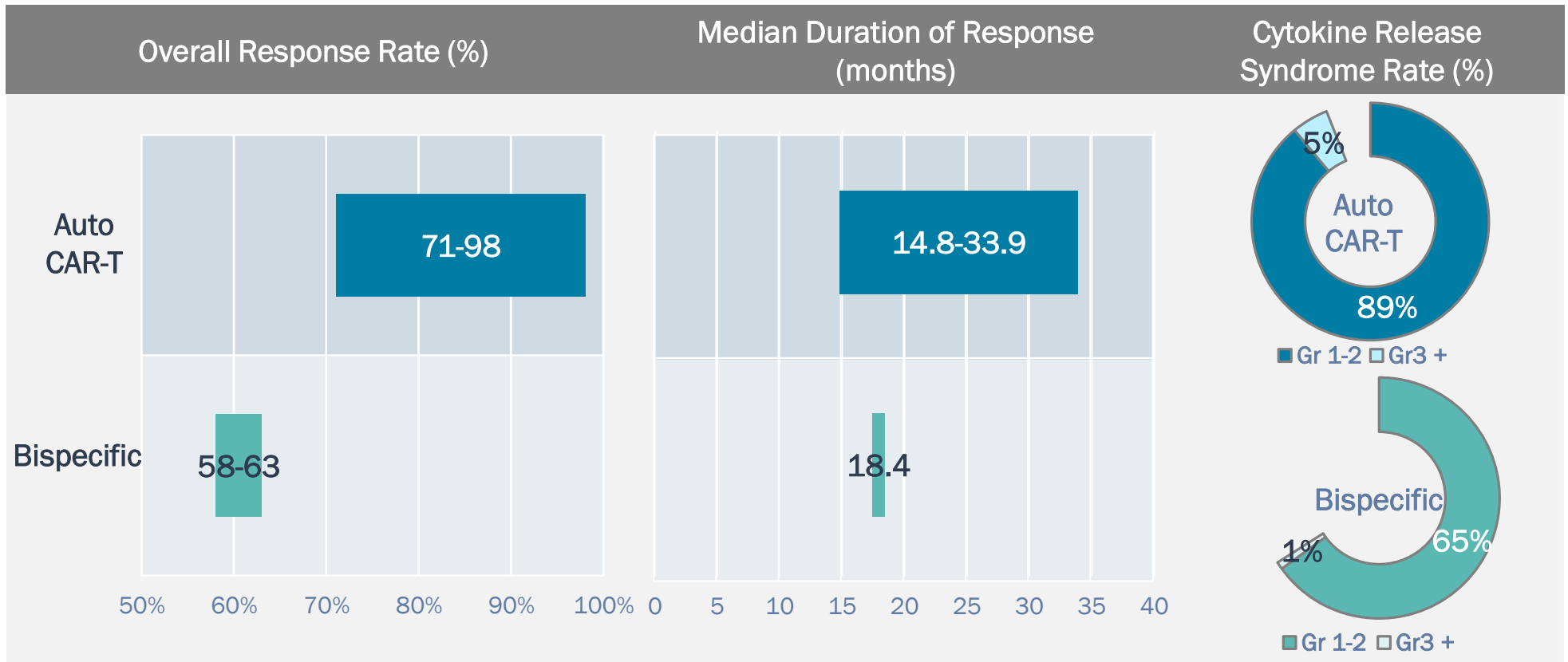
Approved T-Cell Therapies in Multiple Myeloma and Non Hodgkin's Lymphoma

	Therapeutic Class	Drug Name	Sponsor		Indication	
 Multiple Myeloma	Anti-BCMA Auto CAR-T	 CARVYKTI® <small>(ciltacabtagene autoleucl) Suspension for IV infusion</small>			4L+ R/R MM	
		 Abecma™ <small>(idecabtagene vicleucl) SUSPENSION FOR IV INFUSION</small>			4L+ R/R MM	
	Anti-BCMA Bispecific	 TECVAYLI® <small>(teclistamab-cqyv) Injection for subcutaneous use</small>			4L+ R/R MM	
		 ELREXFIO™ <small>(elranatamab-bcmm)</small>			4L+ R/R MM	
 LBCL/ DLBCL	Anti-CD19 Auto CAR-T	 Breyanzi® <small>(tisocabtagene maraleucl) Suspension for IV infusion</small>			2L & 3L LBCL	
		 YESCARTA® <small>(axicabtagene ciloleucl) Suspension for IV infusion</small>			2L & 3L LBCL	
		 KYMRIAH® <small>(tisagenlecleucl) Suspension for IV infusion</small>			3L LBCL	
	Anti-CD20/CD3 Bispecific	 epkinly™ <small>epcoritamab-bysp SUBCUTANEOUS INJECTION 4mg/45mg</small>				3L DLBCL
		 COLUMVI® <small>glofitamab-gxbm Injection for intravenous use 2.5 mg/10 mg</small>				3L LBCL



In MM, bispecifics may lag in ORR compared to auto CAR-T but offer significantly better safety

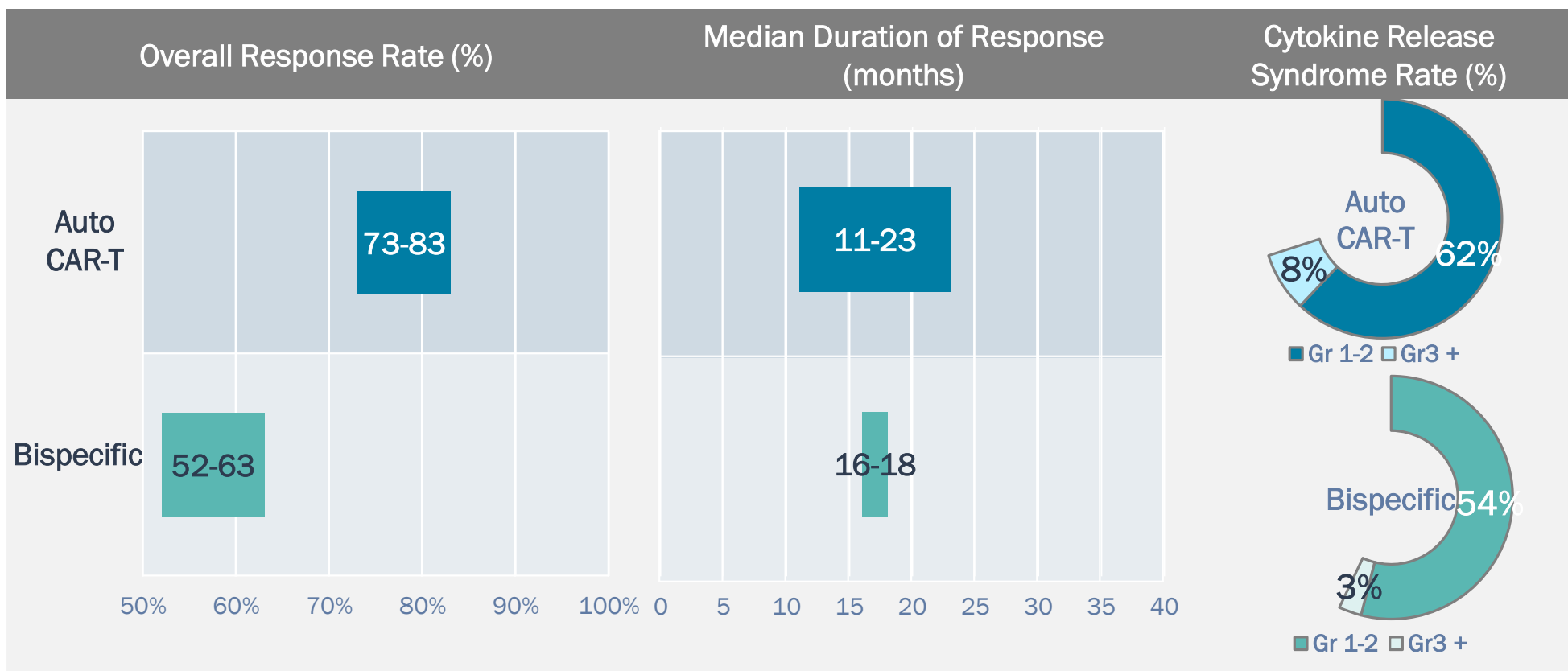
Auto CAR-T vs. Bispecific (Multiple Myeloma)










Similar observations of auto CAR-T and bispecifics in MM hold true for LBCL/DLBCL

Auto CAR-T vs. Bispecific (LBCL/DLBCL)



Long-term follow up and one time treatment favor auto CAR-T over bispecifics; allogeneic CAR-T is aiming to offer the best of both

Comparison of T-cell Based Therapies

	<u>Autologous CAR-T</u>	<u>Bispecific Antibodies</u>	<u>Allogeneic CAR-T (not approved)</u>
 Efficacy	Robust long-term response and durability data ✓	Lower ORR than auto CAR-T; more limited efficacy follow up	?
 Safety/Toxicity	Higher risk of CRS; lower risk of infection	Higher risk of infection; lower risk of CRS ✓	?
 Patient Eligibility	Intensive qualification process and lymphodepletion limit applicability	Broader applicability ✓	Lymphodepletion requirement may limit eligibility
 Turnaround Time	Engineering/quality check processes increase turnaround time	Off-the-shelf capability ✓	Off-the-shelf capability ✓
 Administration	One-time treatment ✓	Requires multiple administrations	One-time treatment ✓

2024 could see the first allo CAR-T pivotal read out; other trials could move auto CAR-T and bispecifics into earlier lines, raising questions about optimal candidates for each and sequencing

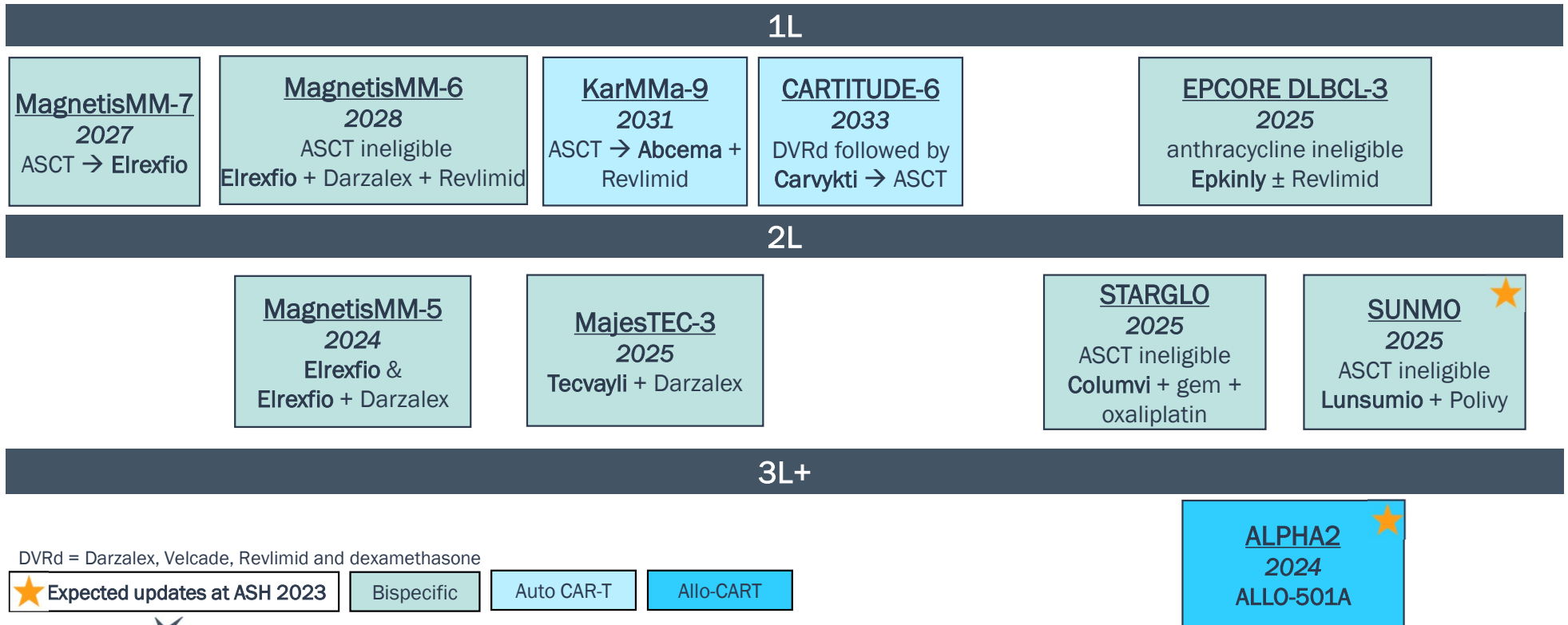
Pivotal Trials to Watch in Multiple Myeloma and LBCL/DLBCL



Multiple Myeloma



LBCL/DLBCL



DVRd = Darzalex, Velcade, Revlimid and dexamethasone

★ Expected updates at ASH 2023
Bispecific
Auto CAR-T
Allo-CAR-T



Source: ASH 2023 Conference Abstracts



ASH 2023 Multiple Myeloma Abstracts to Watch

Target	Abstract #	Title
BCMA	1022	PhI NCT04935580: Dual Targeting BCMA/CD19 Fastcar-T Cells (GC012F) As 1L Therapy for Transplant-Eligible Newly Diagnosed High-Risk MM
	1021	PhII CARTITUDE-2: Cilta cel (BCMA) in MM Patients and 1–3 Prior Lines of Therapy and w/ Early Relapse after 1L Treatment
	3479	PhI NCT04960579: Safety Results of P-BCMA-ALLO1 (Allogeneic CAR-T) in R/R MM Patients
	206	PhII Immuno-PRISM: Teclistamab (BCMA x CD3) in High-Risk Smoldering Myeloma
	1012	PhI NCT04184050: HPN217 (Tri-Specific Targeting BCMA) for R/R MM
GPRC5D	219	PhI Study Updated Results: BMS-986393 (CC-95266), GPRC5D–Targeted CAR-T Therapy for R/R MM
	1014	Ph Ib MonumenTAL-2: Talquetamab (GPRC5D x CD3) + Pomalidomide in R/R MM Patients

CAR-T Bi/Tri-specific



ASH 2023 LBCL/DLBCL Abstracts to Watch

Target	Abstract #	Title
CD20	893	PhII Lysa Study: Glofitamab (CD20 x CD3) in B-NHL after Failing CAR T-Cell Infusion
	438	PhII EPCORE NHL-5 Study: S.C. Epcoritamab (CD20 x CD3) + Lenalidomide in R/R DLBCL
	436	PhII ELM-2 Study: Odronextamab (CD20 x CD3) R/R DLBCL
	855	PhI/II NCT03677154 Study: Mosunetuzumab (CD20 x CD3) + Polatuzumab Vedotin in 1L Elderly Unfit/Frail DLBCL
	613	Ph Ib/II G040516 study: Mosunetuzumab (CD20 x CD3) + Polatuzumab Vedotin in R/R LBCL
	858	PhI/II NCT04980222 Study: Glofitamab (CD20 x CD3) + R-CHOP in 1L High Risk LBCL
CD19	2095	PhI ALPHA and PhI/II ALPHA2 Study: Safety with ALLO-501/501A (CD19) in R/R LBCL and FL

 CAR-T  Bi/Tri-specific

Bluestar BioAdvisors

521 Fifth Ave, 25th floor

New York, NY 10175

Erin Olsen

eolsen@bluestarbio.com

Michelle Whang

mwhang@bluestarbio.com

Elia Farah, PhD

efarah@bluestarbio.com

Darren Eskow

deskow@bluestarbio.com

Monika Trzcinska, PhD

mtrzcinska@bluestarbio.com

Paul Zhang

pzhang@bluestarbio.com