THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Bispecific Antibodies

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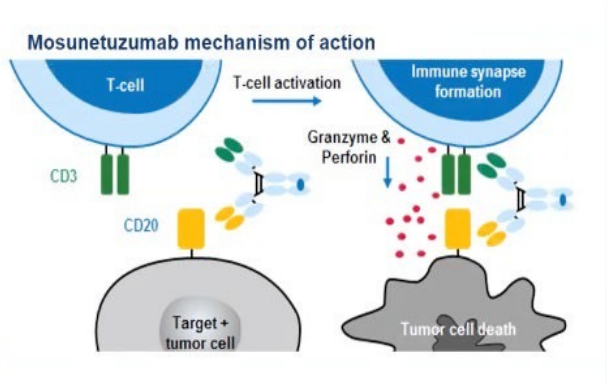
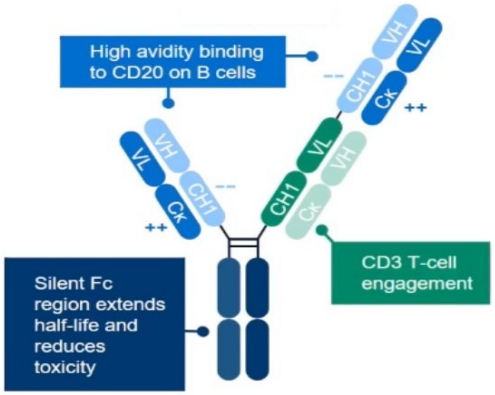
CD3/CD20 Bispecific Antibodies

Mosunetuzumab



IV, SQ

Glofitamab

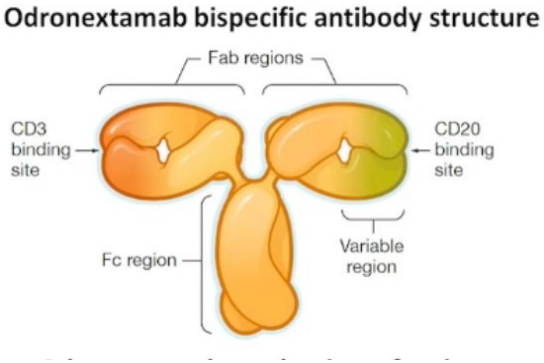


IV

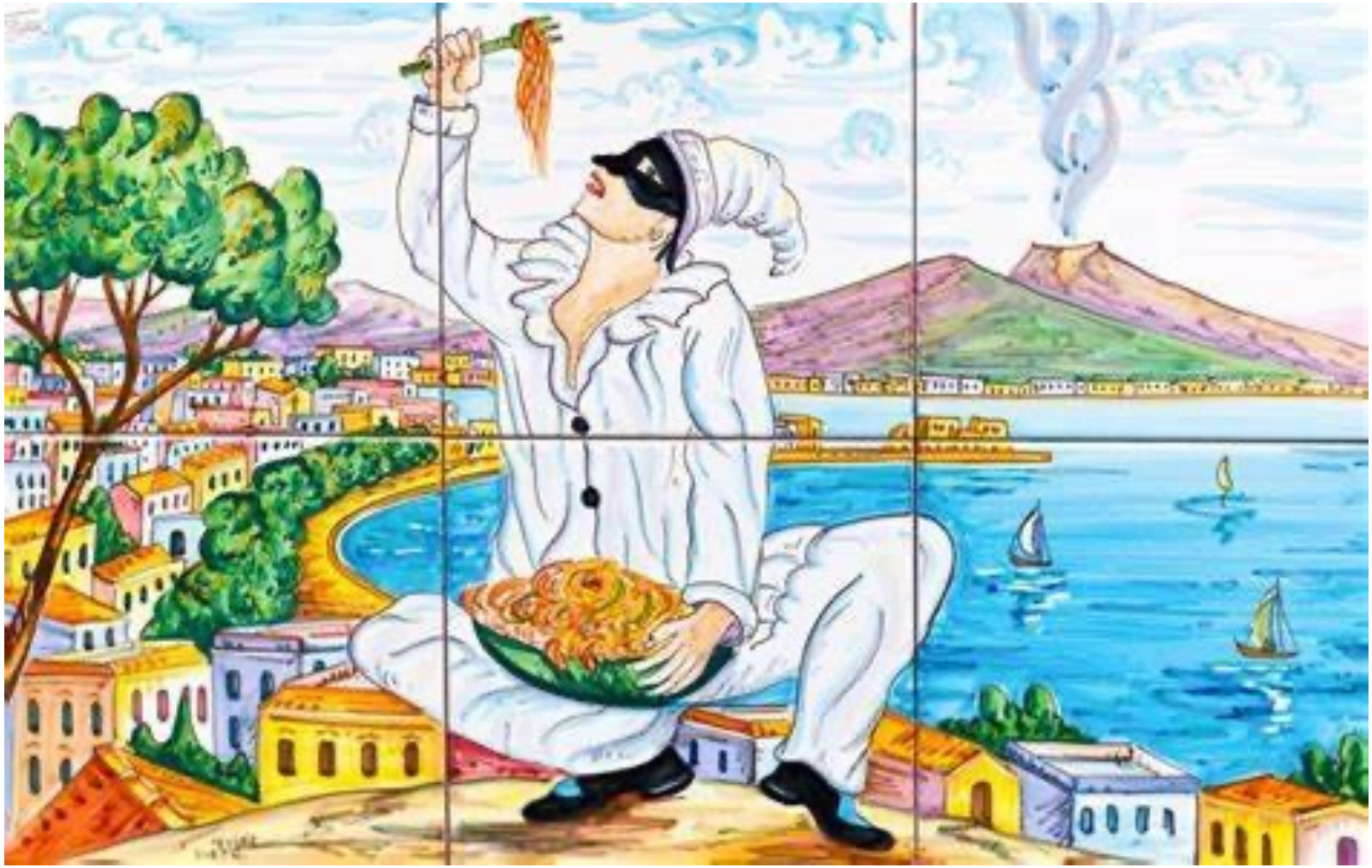
Epcoritamab

SQ

Odronextamab



IV



Pulcinella

Pulcinella

Pulcinella

Pulcinella


J.S. Abramson
Bispecific antibodies remain effective in CAR T exposed patients
Odronextamab
Glofitamab
Epcoritamab
Patients, %
48%
ORR
42%
69%
42%
54%
34%
46%
28%
8th POSTGRADUATE
ABRAMSON

Pulcinella

Some *specific* CD20-CD3 bispecific abs for B-NHL

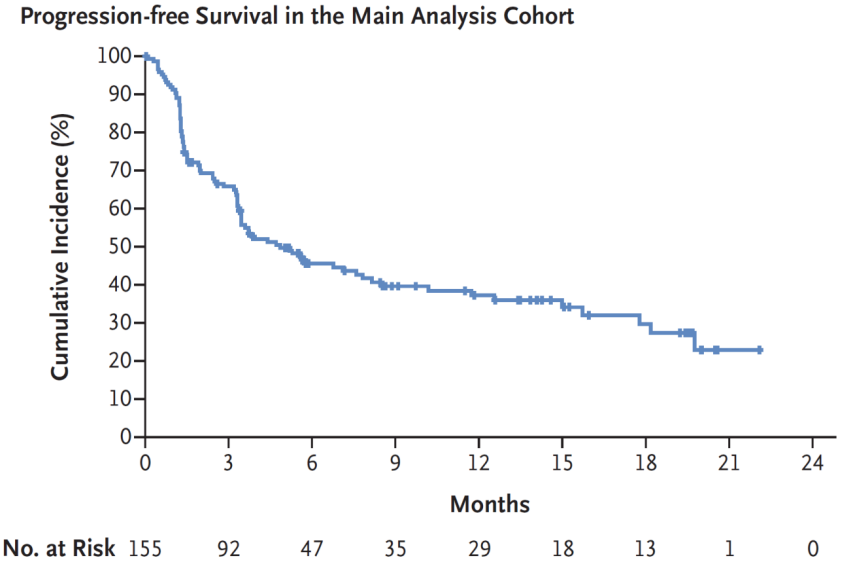
		Odronextamab (Regeneron)	**Mosunetuzumab** (Roche/Genentech)	**Glofitamab** (Roche)	**Plamotamab** (Xencor)	**Epcoritamab** (AbbVie/Genmab)
	Study Phase	**Phase 1/2**	**Phase 1/1b**	**Phase 1b**	**Phase 1**	**Phase 1/2**
	Study Population	R/R B-NHL patients with aggressive disease after at least 2 prior therapies	R/R NHL patients with at least 2 prior therapies	R/R NHL patients with aggressive disease after at least 1 prior systemic therapy	Transplant ineligible R/R NHL patients	R/R DLBCL and aggressive NHL patients after anti-CD20 treatment and/or ASCT
	Administration	IV	IV	IV	IV	SC
	Sample Size	DLBCL = 71 FL = 37	DLBCL = 119 FL = 62	DLBCL = 85, FL = 18 (fixed dosing)	DLBCL = 18 FL = 5	DLBCL = 46 FL = 12
Efficacy	**DLBCL: ORR, CR, mDoR/DoCR**	60% ORR, 60% CR, mDOR 10.3 mo, mDoCR 9.5 mo	35% ORR, 19% CR	49% ORR, 34% CR, mDoCR NR	39% ORR, 28% CR	68% ORR, 46% CR (dose 12-60 mg)
Efficacy	**FL: ORR, CR, mDoR/DoCR**	93% ORR, 75% CR, mDOR 7.7 mo, mDoCR 8.1 mo	68% ORR 50% CR, mDoR 20.4 mo	67% ORR, 50% CR, mDoR NR	ORR N/A, 20% CR	80% ORR, 60% CR (dose 12-48 mg)
Safety	**All CRS**	62%	28.4% (Group B); 23% (FL population)	56%	56%	59%
Safety	**Grade 3+ CRS**	7%	1.4%; 6%	2%	4%	0%

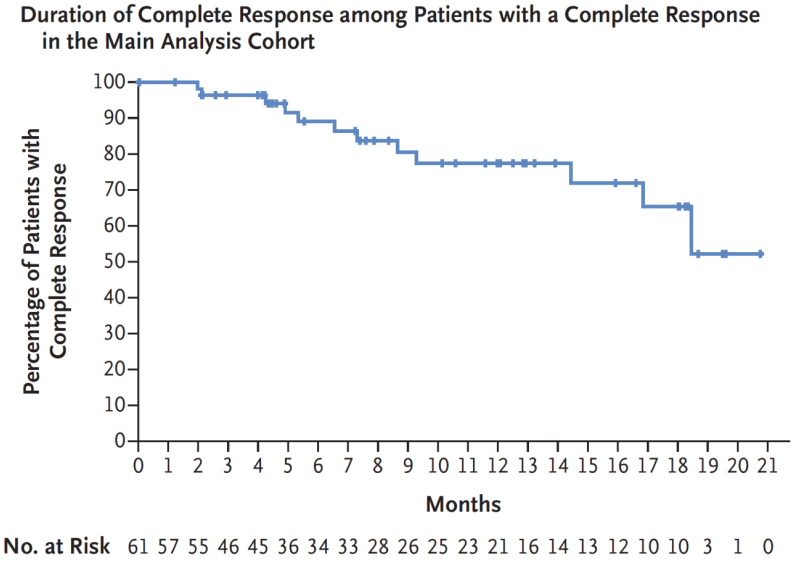
Overview: CD20-CD3 bispecifics

- CD20-CD3 bispecific monotherapy CR in R/R B-cell NHL including:
  - Prior CAR-T therapy
  - DLBCL with prior ASCT and/or CD20-refractory disease
  - Poor-risk Indolent NHL
    - CD20- and alkylating agent-refractory disease
    - history of POD24 months
- CRs have been maintained after completion of therapy
- CRS may reduce with step up dosing and SC administration
- Single-agent and combination studies ongoing

DLBCL Glofitamab: Key Efficacy

	Independent Review (n = 155)	Investigator Review (n = 155)
Complete response, % (95% CI)	39 (32–48)	37 (30–46)
Overall response, % (95% CI)	52 (43–60)	57 (49–65)
PFS median (95% CI) – mo	4.9 (3.4–8.1)	3.8 (3.3–5.4)
OS median (95% CI) – mo	—	11.5 (7.9–15.7)





Dickinson, et al. *N Engl J Med.* 2022.

DLBCL Glofitamab: Common AEs

Event	Number (%)
CRS, per ASTCT	97 (63)
Most common grade 3 or 4 adverse events	
Neutropenia	41 (27)
Anemia	10 (6)
Thrombocytopenia	12 (8)
Any glofitamab-related grade 3 or 4 adverse event	64 (42)
AEs of Interest	
Sepsis	6 (4)
Tumor flare	5 (3)
Infection, any grade	59 (38)
Event grade consistent with ICANS, any grade	12 (8)

Dickinson, et al. *N Engl J Med.* 2022.

Bispecific Ab Mosunetuzumab in R/R FL

Phase 2 Pivotal Study

N=90

- Patients aged ≥18 yr with R/R FL grades 1-3a
- CD20+
- ECOG PS ≤1
- ≥2 prior systemic therapies including ≥1 anti-CD20 antibody and ≥1 alkylating agent

Cycle 1 (21-Day Cycles)*	Cycle 2	Cycles 3-8
Mosunetuzumab D1: 1 mg; D8: 2 mg; D15: 60 mg	**Mosunetuzumab** D1: 60 mg	**Mosunetuzumab** D1: 30 mg

*Cycle 1 step-up dosing for CRS mitigation.

Discontinue if CR by cycle 8; if PR or SD, continue treatment for 17 cycles, unless PD or unacceptable toxicity occurs

Primary endpoints
CR (best response) rate by IRF, assessed vs 14% historical control CR rate
Secondary endpoints
ORR, DoR, PFS, safety and tolerability

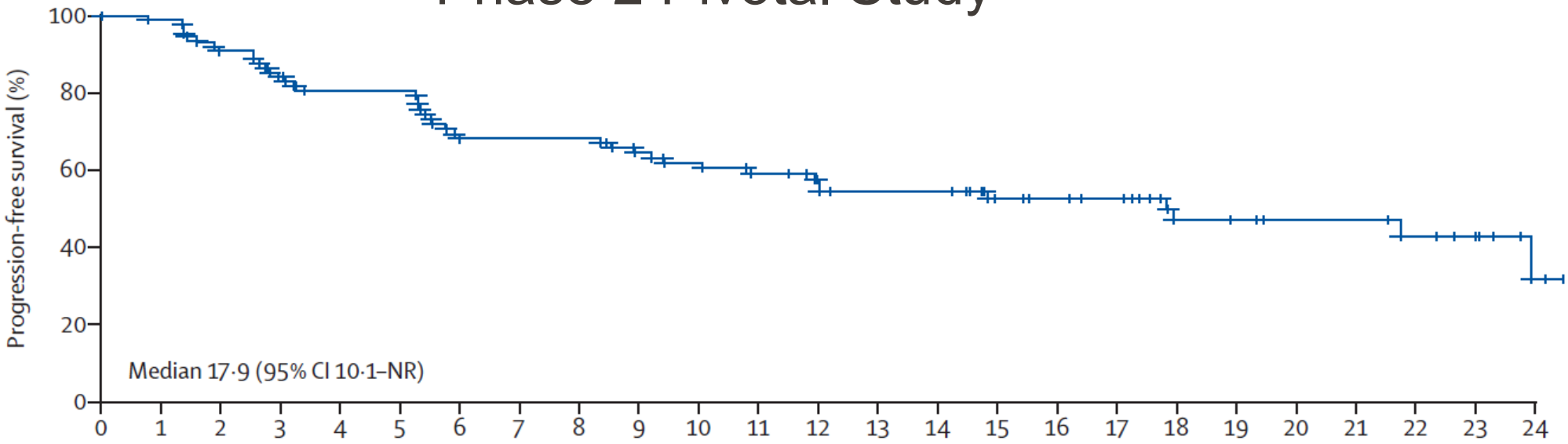
Outcome, % (95% CI)	By IRF (N = 90)	By INV (N = 90)
ORR ▪ CR	80 (70-88) 60 (49-70)	78 (68-86) 60 (49-70)

Response by Double Refractory Disease Status, % (95% CI)[1]	Yes (n = 48)	No (n = 42)
ORR ▪ CR	71 (56-83) 50 (35-65)	90 (77-97) 71 (55-84)
Response by POD ≥24 Mo of Initial Tx, % (95% CI)[1]	Yes (n = 47)	No (n = 43)
ORR ▪ CR	85 (72-94) 57 (42-72)	74 (59-86) 63 (47-77)

Budde LE et al. *Lancet Oncol*. 2022;23(8):1055-1065.

Bispecific Ab Mosunetuzumab in R/R FL

Phase 2 Pivotal Study



	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Number at risk	90	87	80	73	66	66	56	55	55	50	46	43	39	35	35	28	26	24	15	14	12	12	10	8	3
(number censored)	(0)	(2)	(2)	(3)	(7)	(7)	(8)	(8)	(8)	(10)	(12)	(13)	(16)	(18)	(18)	(24)	(26)	(28)	(35)	(36)	(38)	(38)	(39)	(41)	(45)

CRS was the most common AE (40 [44%] of 90 patients) and was predominantly grade 1 (23 [26%] of 90) and grade 2 (15 [17%]), and primarily confined to cycle 1

The most common grade 3-4 AEs were neutropenia or neutrophil count decreased (24 [27%] of 90 patients), hypophosphataemia (15 [17%]), hyperglycaemia (seven [8%]), and anaemia (seven [8%]); Serious adverse events occurred in 42 (47%) of 90 patients.

Budde LE et al. *Lancet Oncol*. 2022;23(8):1055-1065.

Primary results: Comparison of GO29781 to LEO CReWE Cohort

Group	N (Evaluable for Response)	ORR (95% CI)	CR Rate (95% CI)	PFS12 (95% CI)
LEO CReWE (unweighted)	202 (192)	77.6 (70.9-83.2)	57.8 (50.5-64.8)	65.0 (58.6-72.2)
LEO CReWE (MAIC Weighted)	167 (160)	73.0 (65.3-79.5)	52.9 (44.8-60.7)	59.5 (51.0-69.3)
GO29781 (trial results)	90 (90)	80.0 (70.3-87.7)	60.0 (49.1-70.2)	57.7 (46.9-68.4)
ORR=overall response rate; CR=complete response; PFS12=progression free survival at 12 months				

Maurer et al. *Haematologica*, 2023

CAR T-cell therapy and bispecific antibodies for R/R DLBCL

	CAR T-Cell Therapy			Bispecifics			
	Axi-cel (Gilead/Kite)	**Tisa-cel** (Novartis)	**Liso-cel** (BMS)	**Glofitamab** (Roche)	**Odronextamab** (Regeneron)	**Mosunetuzumab** (Roche/Genentech)	**Epcoritamab** (AbbVie/Genmab)
Patient Population	R/R DLBCL patients after ≥ 2 prior therapies	R/R DLBCL patients after ≥ 2 prior therapies	R/R large B-cell lymphoma patients after ≥ 2 prior therapies	R/R aggressive NHL patients after ≥ 1 prior therapies	R/R aggressive DLBCL patients after ≥ 2 prior therapies	R/R NHL patients with at least 2 prior therapies	R/R DLBCL and aggressive NHL patients after anti-CD20 treatment and/or ASCT
Trial	NCT02348216 ZUMA-1, P1/2	NCT02445248 JULIET, P2	NCT02631044 TRANSCEND NHL-001, P1	NCT0307569 6 NP30179, P1	NCT02290951, P1	NCT02500407 GO29781, P1/1b	NCT03625037 P1/2
Efficacy	CR: 51% ORR: 72%	CR: 32% ORR: 50%	54% CR 73% ORR .	CR: 34% ORR: 49%	CR: 60%[b] ORR: 60%[b]	CR: 19% ORR: 35%	CR: 68% ORR: 46% (dose:12-60 mg)
Safety (Severe AEs)	CRS: 94% (13% grade 3+) Neutropenia: 31%	CRS: 74% (grade 3+:23%) Grade 3+ Neutropenia: 17%	CRS: 46% (grade 3+: 4%) Grade 3+ Neutropenia: 76%	CRS: 56.4% Neutropenia: 30.8%	CRS: 62.2% (7.1% grade 3+) Gr 3 neurologic AEs : 4%	CRS: 28.4% (Total pollution in Group B of study)	CRS: 59% (Total population); no Grade ≥ 3 CRS events

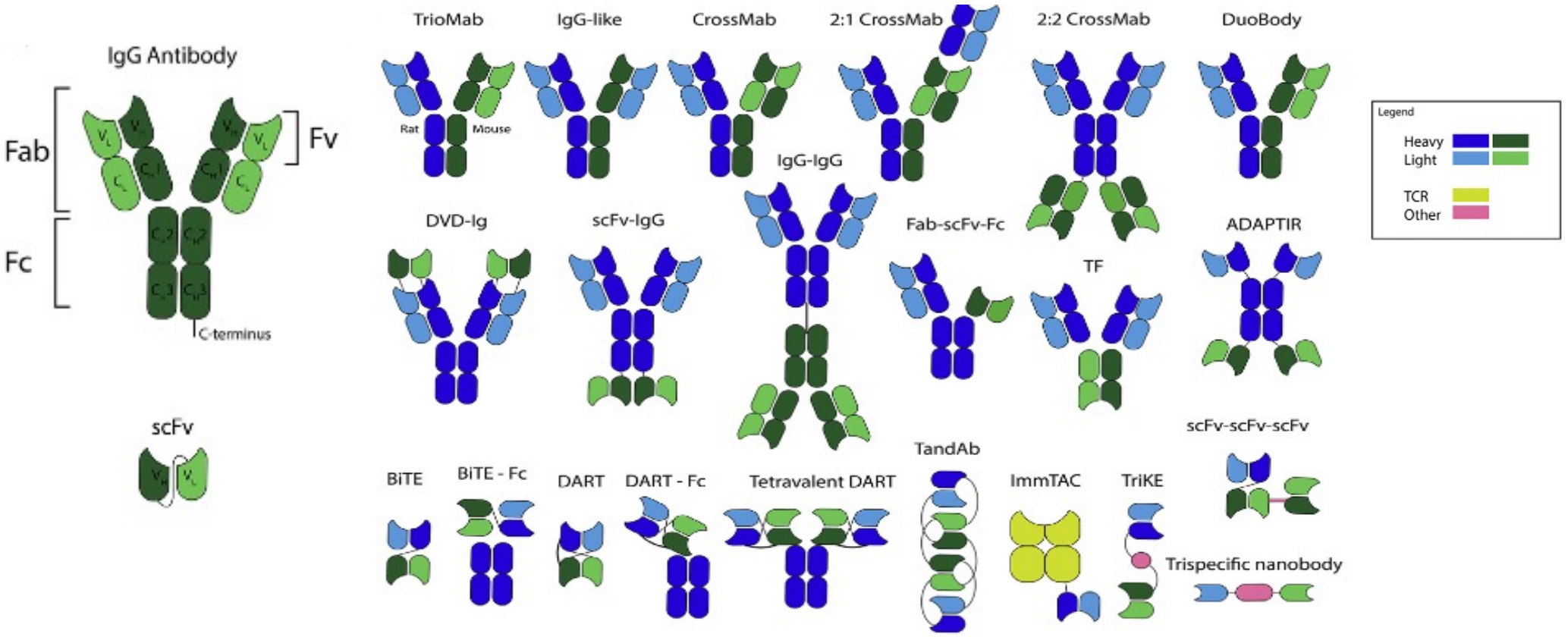
CAR T-cell therapy and bispecific antibodies for R/R FL

	CAR T-Cell Therapy			Bispecifics			
	Axi-cel (Gilead/Kite)	**Tisa-cel** (Novartis)	**Liso-cel** (BMS)	**Glofitamab** (Roche)	**Odronextamab** (Regeneron)	**Mosunetuzumab** (Roche/Genentech)	**Epcoritamab** (AbbVie/Genmab)
Patient Population	R/R FL patients after ≥ 2 prior therapies	R/R FL patients after ≥ 2 prior therapies	R/R LBCL patients after ≥ 2 prior therapies (FL grade 3B)	R/R NHL patients after ≥ 2 prior therapies	2L+ Indolent B-cell NHL (prior CD20 treatment)	R/R aggressive NHL patients after ≥ 1 prior therapies	Aggressive NHL patients after anti-CD20 treatment and/or ASCT
Trial/Phase	NCT03105336 ZUMA-5, P2	NCT03105336 ELARA, P2	NCT02631044 TRANSCEND NHL-001, P1	NCT02500407 GO29781, P1/1b	NCT02290951, P1	NCT03075696 NP30179, P1	NCT03625037 P1/2
Efficacy	CR: 80% ORR: 95%	CR: 65% ORR: 83% (ITT population)	54% CR 73% ORR mDOR: 16.7 mo.	CR: 50% ORR: 68%	CR: 75% ORR: 93%	CR: 50% ORR: 67%	CR: 60% ORR: 80% (dose ≥ 12 mg)
Safety (Severe AEs)	CRS: 84% (8% grade 3+) Neutropenia: 41% (for all patients with iNHL)	CRS: 48% Grade 3+ Neutropenia: 28% Serious Neurologic Events:10%	CRS: 46% (grade 3+: 4%) Grade 3+ Neutropenia: 76%	CRS: 23% (SAE CRS: 6%) Hypophos: 23% Neutropenia: 21%	CRS: 62.2% (7.1% grade 3+) Gr 3 neurologic AEs: 4%	CRS: 56.4% Neutropenia: 30.8%	CRS: 59% (Total population); no Grade ≥ 3 CRS events

Pro: CD20-CD3 bispecifics

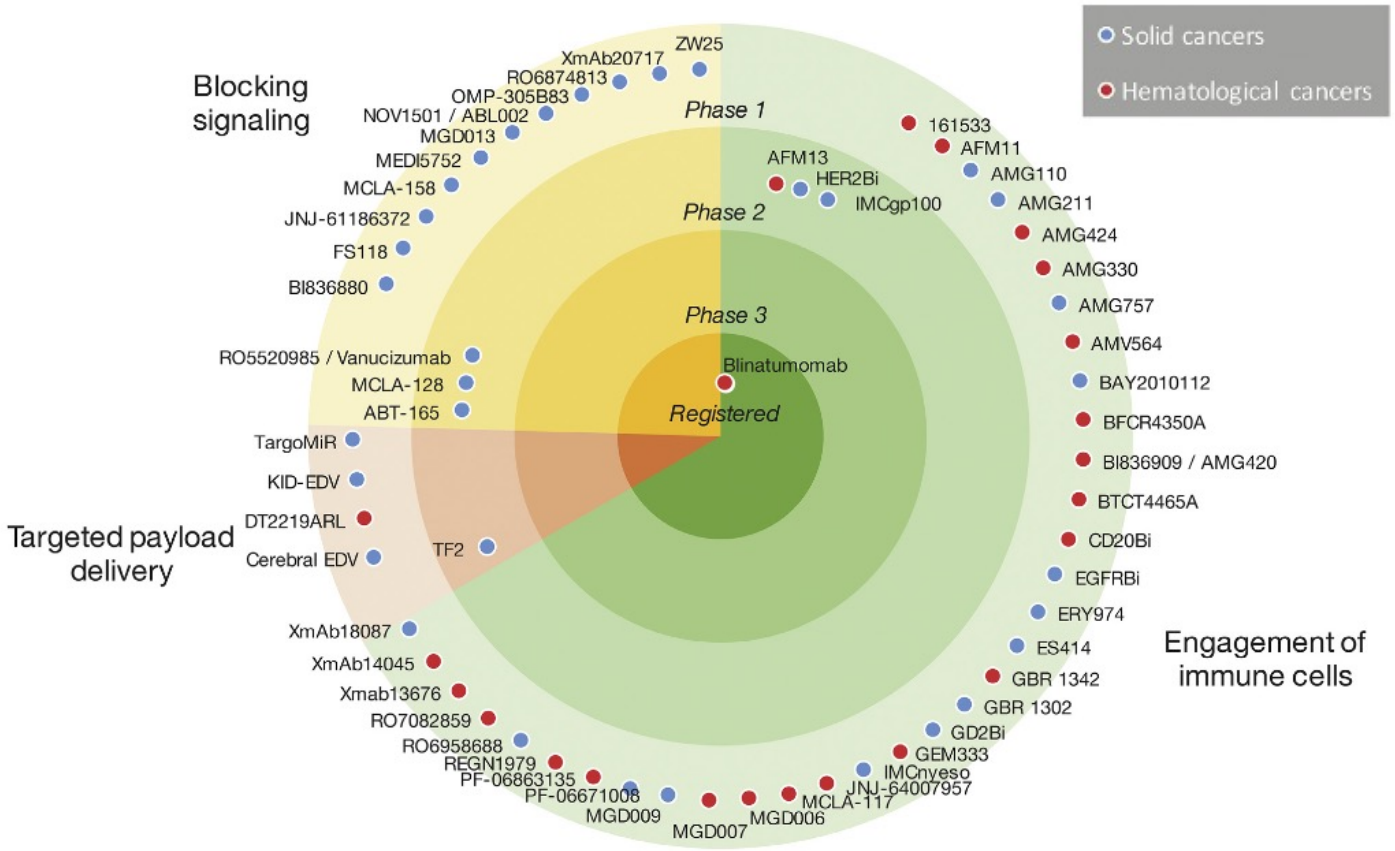
- CD20-CD3 bispecific monotherapy produce durable CR in R/R NHL:
  - Effective Prior to and Post CAR-T therapy
  - Only time-limited therapies can produce cure
  - CRs have been maintained after completion of therapy
- More easily administered in clinical practice
  - Lower rates of CRS, ICANS
  - Easier to coordinate access to therapy
  - CRS may reduce with step up dosing and SC administration
- Single-agent and combination studies ongoing to allow more options

Bispecific Antibody Constructs



Suurs et. al. Pharmacology & Therapeutics. 2019

Bispecific Abs in Development



Suurs et. al. Pharmacology & Therapeutics. 2019

Maradona

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Question

- What is the ORR and CR in R/R FL for patients receiving mosunetuzumab?
  A. 50% and 20%
  B. 60% and 30%
  C. 70% and 40%
  D. 80% and 50%
  E. 80% and 60%