Novel Bispecific Antibodies for Follicular lymphoma

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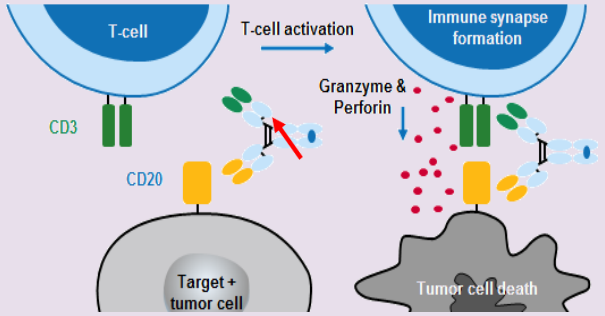
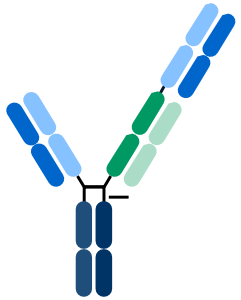
Bispecific antibodies in development

Mosunetuzumab (CD3xCD20)

FDA Approved Dec 2022

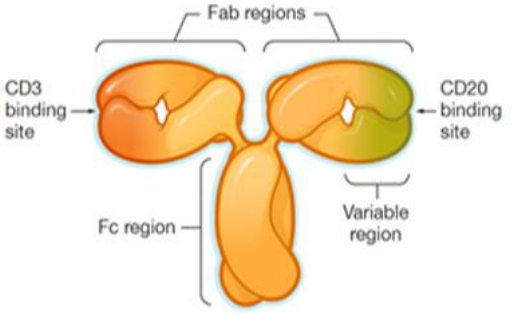


Glofitamab (CD3xCD20)

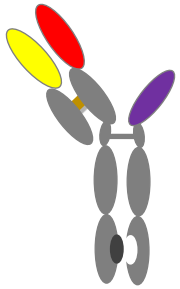


Epcoritamab (CD3xCD20)

Odronextamab (CD3xCD20)



TNB-486 (CD3x**CD19**)

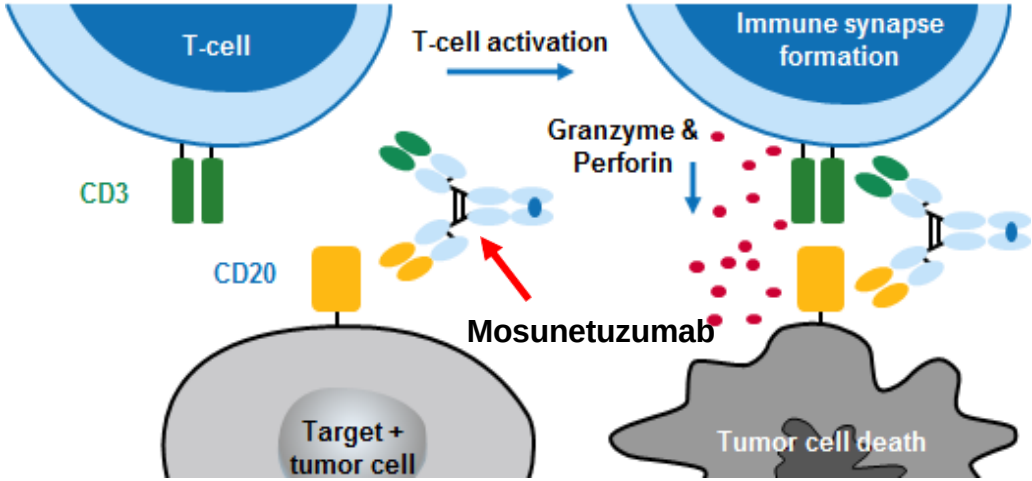


Fc Tail

Plamotamab (CD3xCD20)

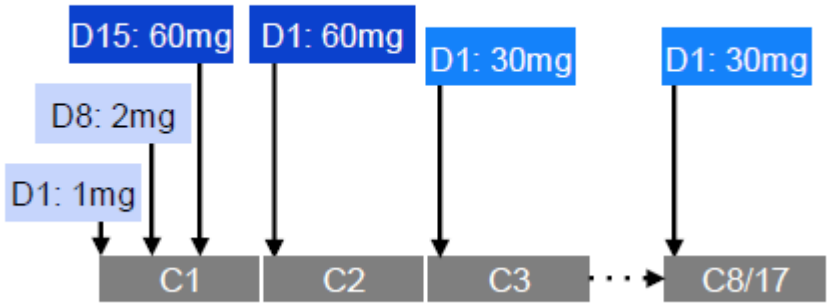
Mosunetuzumab (CD20 x CD3 T-cell Engager: First FDA approved bispecific antibody for R/R FL (Dec 2022)

- Mosunetuzumab **(first-in-class)** is now FDA approved for the treatment of **relapsed/refractory follicular lymphoma (R/R FL)** after ≥2 prior systemic therapies.
- Redirects T cells to engage and eliminate malignant B cells
- Off the Shelf outpatient treatment



Mosunetuzumab administration

- IV mosunetuzumab administered in 21-day cycles with step-up dosing in C1
- Fixed-duration treatment: 8 cycles if CR after C8; 17 cycles if PR/SD after C8
- Re-treatment with mosunetuzumab permitted at relapse for patients who achieved CR
- No mandatory hospitalization



Bartlett et al. ASH 2022; Budde et al. The Lancet Oncology 2022; Sun LL, et al: Sci Transl Med 2015;7:287ra70; Hernandez G, et al. ASH 2019

Mosunetuzumab:
Baseline characteristics: Heavily pretreated patients

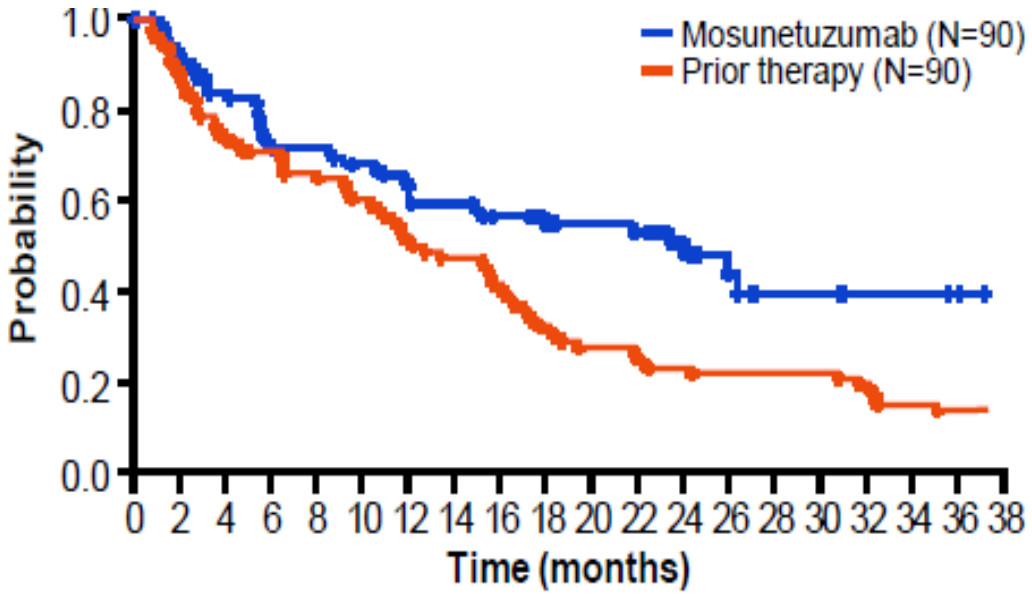
	N=90
Median age, years (range)	60 (29–90)
Male	61%
ECOG PS	
0	59%
1	41%
Ann Arbor stage	
I/II	23%
III/IV	77%
Median lines of prior therapy, n (range)	3 (2–10)
Refractory to last prior therapy	69%
Refractory to any prior anti-CD20 therapy	79%
Progression of disease within 24 months from start of first-line therapy (POD24)	52%
Double refractory to prior anti-CD20 and alkylator therapy	53%
Prior autologous stem cell transplant	21%

Bartlett et al. ASH 2022; Budde et al. The Lancet Oncology 2022;

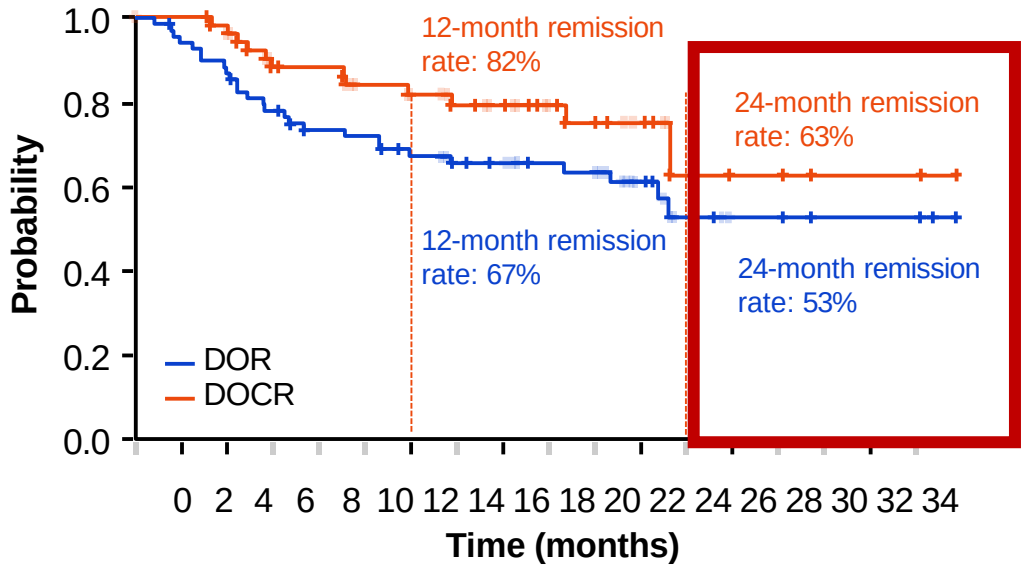
Mosunetuzumab: Efficacy Analysis

ORR	**78%**
CR	**60%**
Median FU	**28.3**

mPFS: 24 months



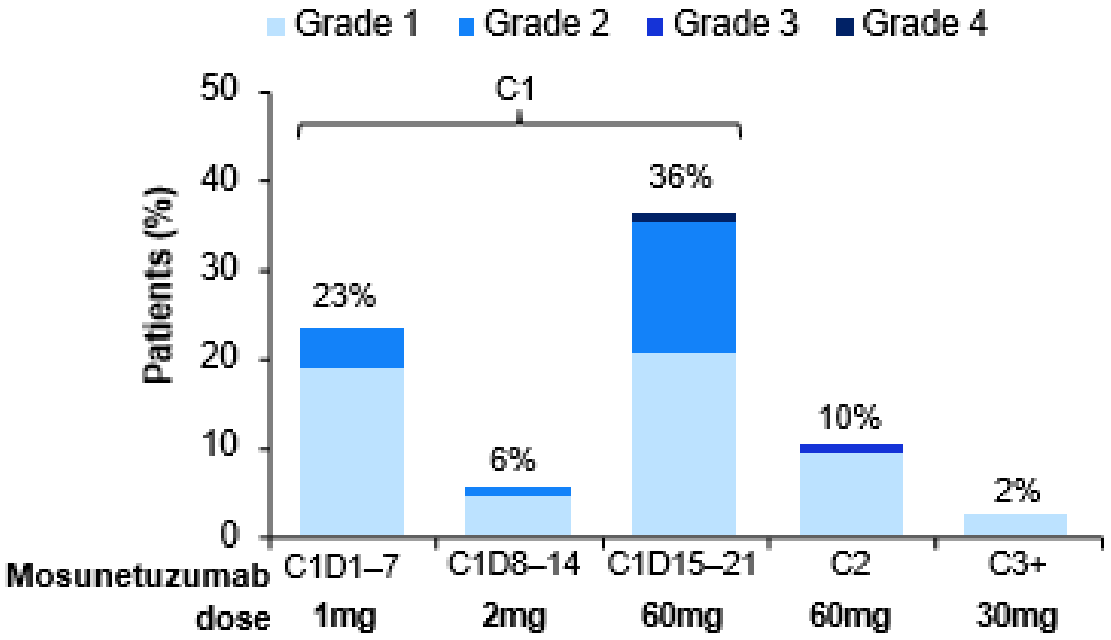
mDOR: NR and mDOCR: NR



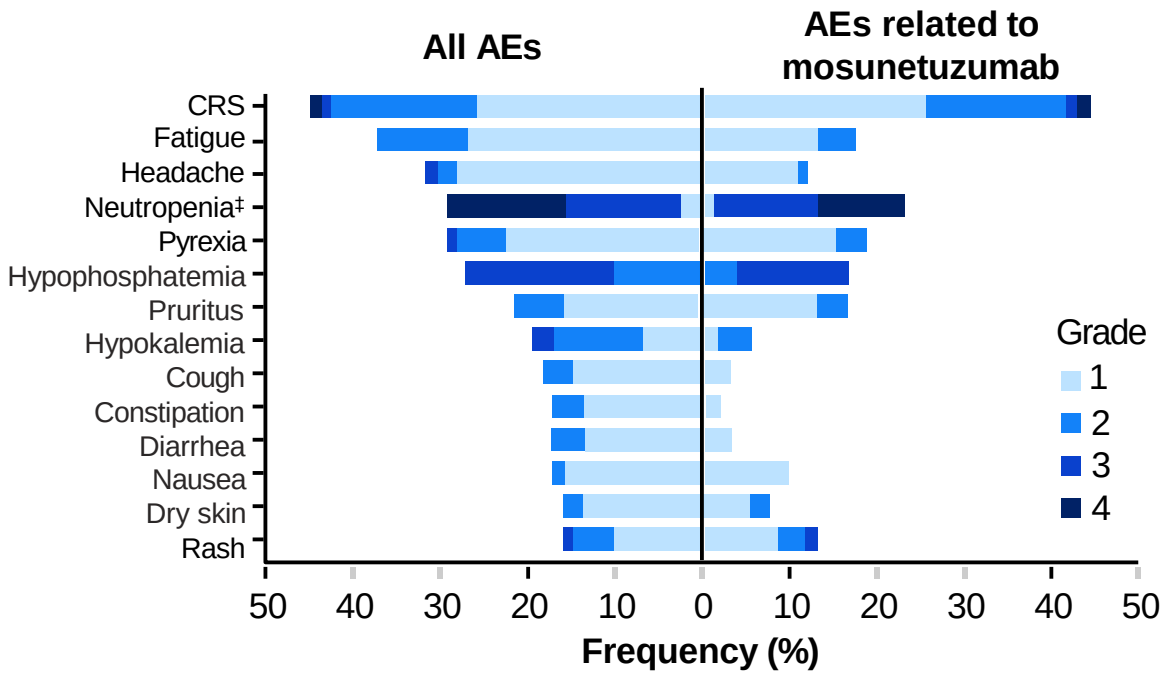
Bartlett et al. ASH 2022; Budde et al. The Lancet Oncology 2022

Mosunetuzumab: Safety profile

CRS by cycle and grade



AEs (≥15%) by grade and relationship with mosunetuzumab



CRS mostly low grade (Grade 3/4: 2%) and occurred during Cycle 1
ICANs 3% (all grade 1-2)

Bartlett et al. ASH 2022; Budde et al. The Lancet Oncology 2022;

Other Bispecifics (CD3/CD20)

Glofitamab in R/R FL	Epcoritamab + Rituximab + Lenalidomide in R/R FL	Odronextamab in R/R FL
Phase I/II	Phase I/II (EPCORE NHL-2)	Phase 2 (ELM-2)
Monotherapy or combination with obinutuzumab	Combined with R2	Monotherapy
Intravenous	Subcutaneous	Intravenous
C1: D1, 8, 15 then q21 days	Weekly first 2 cycles Afterwards Q21 days	C1: D1/2, 8/9, 15 Cycles 2-4: D1,8,15 then maintenance Q2w
Fixed duration: 12 cycles	Up to 2 years	Till disease progression

Morschhauser et al. ASH 2021 (Glofitamab); kim et al. ASH 2022 (Odronextamab); Falchi et al. ASH 2022 (Epcoritamab)

CAR-T vs Bispecifics

	Axi-cel	Tisa-cel	Mosunetuzumab (CD3xCD20)	Odronextamab (CD3xCD20)	Epcoritamab + R2 (CD3xCD20)	Glofitamab (CD3xCD20)
ORR %	94%	86%	78%	82%	95%	81%
CR %	79%	68%	60%	75%	80%	70%
mPFS	39.6%	Not reached	24 mo	20.2 mo	Not reached	Not reported
mDOR	38.6%	Not reached	Not reached	20.5 mo	Not reached	Not reported
CRS **Gr 1-2** **Gr 3-4**	 72% (1-2) 6% (3-4)	 48.5% (1-2) 0% (3-4)	 43% (1-2) 2% (3-4)	 56% (1-2) 1.6% (3)	 43% (1-2) 0% (3-4)	 55% (1-2) 0% (3-4)
ICAN (Neuro toxicity) **Gr 1-2** **Gr ≥ 3**	 41% 15%	 12% 1 %	 3% (1-2) 0%	 1.5% 0%	 1/76 pts (Gr 1) 0%	 0% 0%
Duration of therapy	One time!	One time!	8-17 cycles	Till PD	Up to 2 years	12 cycles
Median follow-up	31 mo	28.9%	28.3 mo	17.3 mo	6.4 mo	4.4

Neelapu et al. ASH 2021 (Axi-cel); Dreyling et al. ASH 2022 (Tisa-cel); Budde et al. The Lancet Oncology 2022 (Mosunetuzumab); Morschhauser et al. ASH 2021 (Glofitamab); kim et al. ASH 2022 (Odronextamab); Falchi et al. ASH 2022 (Epcoritamab)

Thank you!!

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