Bispecific antibodies in FL

6th Postgraduate Lymphoma Conference

Rome, 09 September 2022

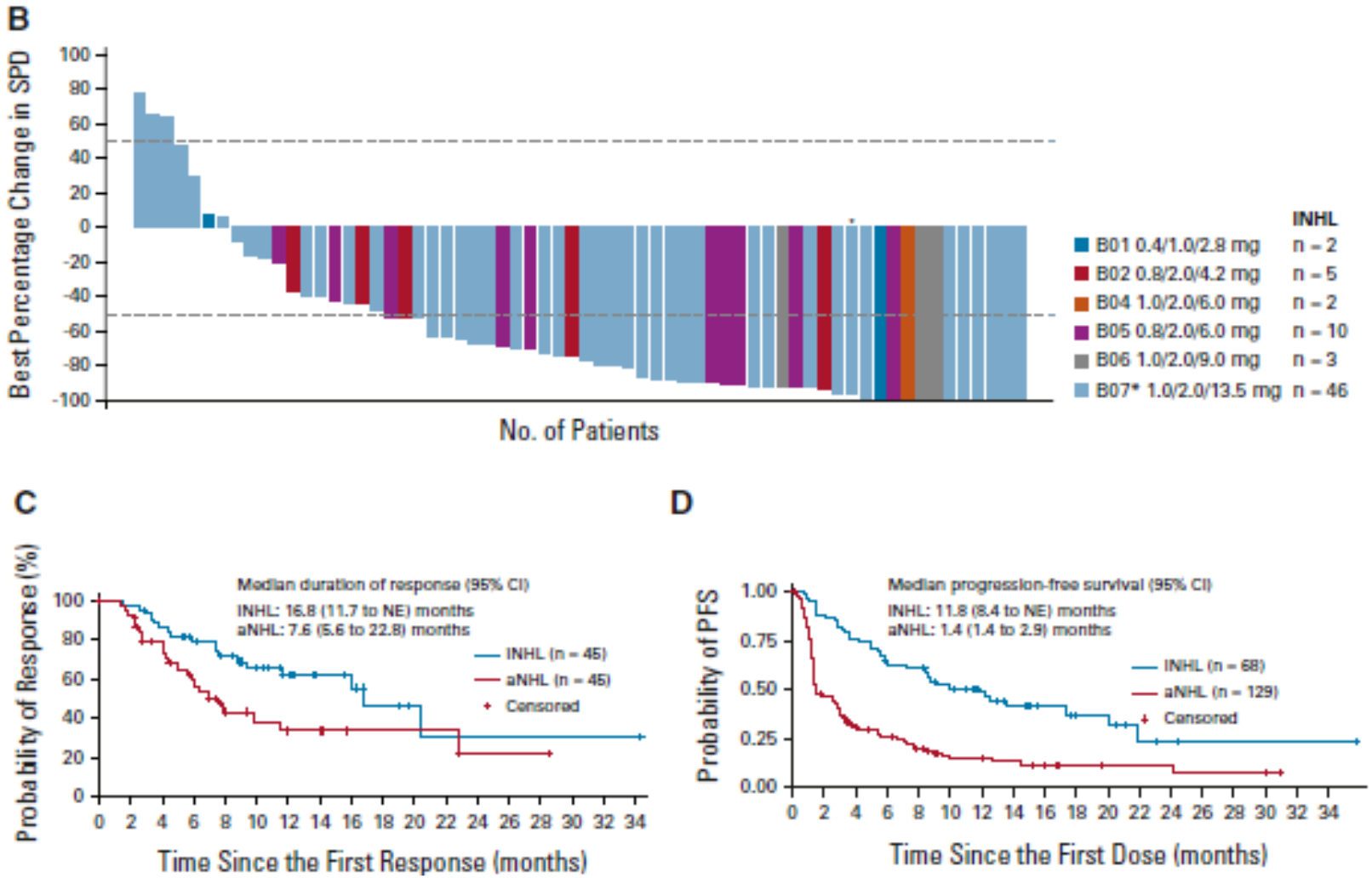
Martin Hutchings
Department of Haematology and Phase 1 Unit
Rigshospitalet, Copenhagen, Denmark

DISCLOSURES

- **Scientific advisory boards:**
  - AbbVie, Celgene, Genmab, Janssen, Merck, Roche, Takeda
- **Research support (institution):**
  - Celgene, Genentech, Genmab, Incyte, Janssen, Novartis, Roche, Takeda

Single-agent phase 1 studies of bispecific CD3/CD20 antibodies in B-NHL

Activity of mosunetuzumab in r/r indolent B-NHL in the phase 1 study

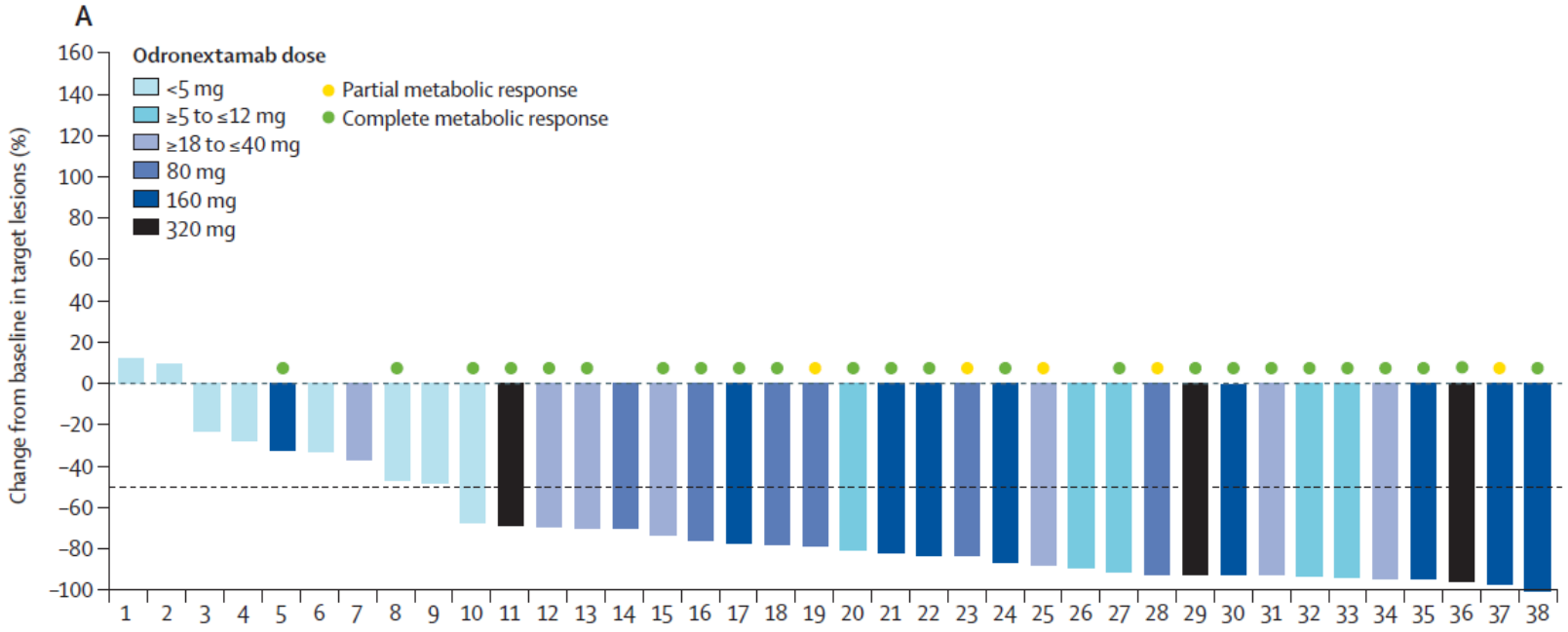


68 iNHL patients, of whom 65 had FL grade I-IIIA

- Treated across dose levels of 2.8 mg or higher:
- ORR 66% in R/R iNHL
- CRR 35% in R/R iNHL
- CRS in just 27% of patients
- No mandatory hospitalisation

Budde LE, et al. J Clin Oncol 2021; 40: 481-91.

Activity of odronextamab in r/r indolent B-NHL in the phase 1 study



- Odronextamab given in 3-week cycles:
- Step-up treatment in cycle 1 on days 1, 2, 8, 9, 15, and 16
- 24h hospitalization after each treatment, at least until after the first full cycle on C2D1

40 FL grade I-IIIA patients

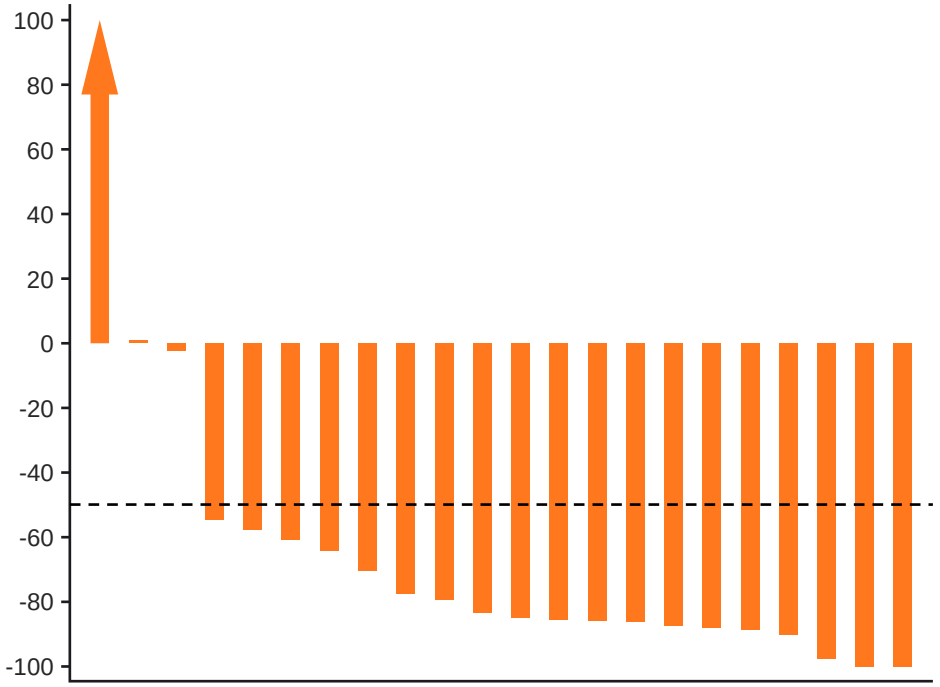
- Treated across all dose levels
- ORR 78%
- CRR 63%
- CRS in 61% of patients
  - incl. 7% with CRS grade 3-4
- DoR 10.4 months
- DoCR 14.5 months

In 32 iNHL patients treated at dose levels of 5 mg or higher:

- ORR 91%
- CRR 72%

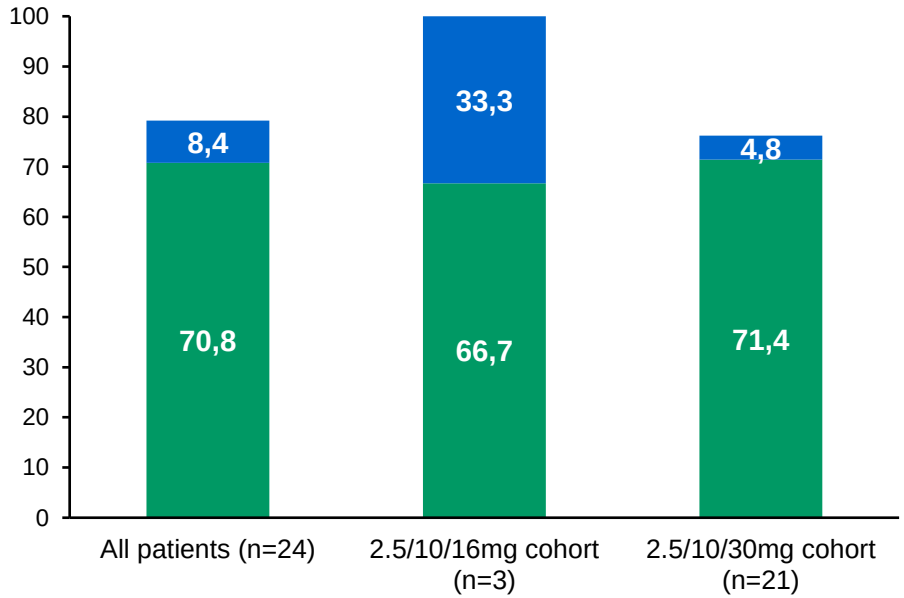
Bannerji R, et al. Lancet Haematol 2022; 9 : e327–39

Activity of glofitamab in r/r indolent B-NHL in the phase 1 study



Glofitamab at RP2D (16 or 30 mg) in grade 1-3a r/r FL[1,2]

- ORR 79%
- CRR 71%
- CRS in 67% of patients, incl. 5% with grade 3-4

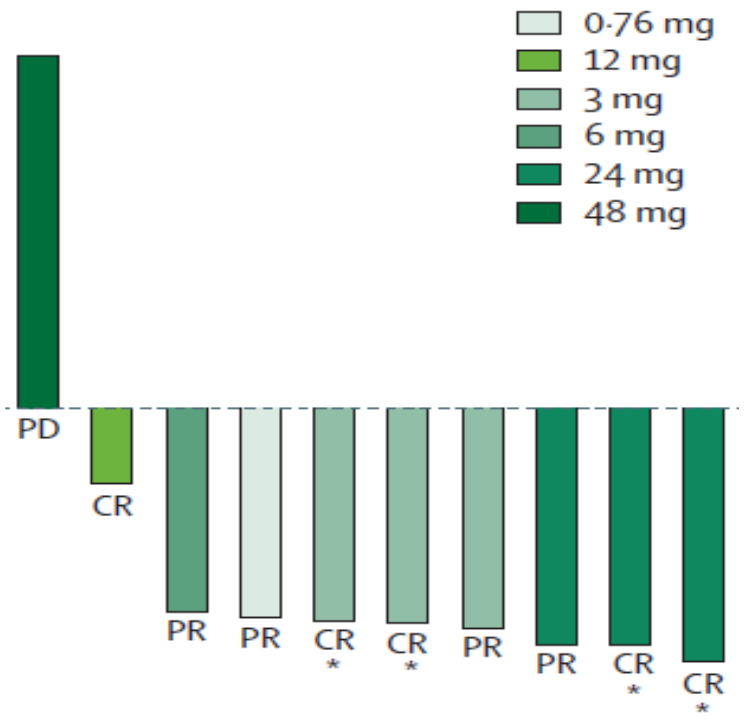


1. Hutchings M, *et al. J Clin Oncol* 2021; **39**:1959–1970; 2. Carlo-Stella C, *et al.* ICML 2021. Abstract 15 (oral).

Activity of epcoritamab in r/r FL in the phase 1 study

Epcoritamab at doses 0.76 – 48 mg in r/r FL

- ORR 90%
- CRR 50%
- CRS in 66% (all grade 1-2)



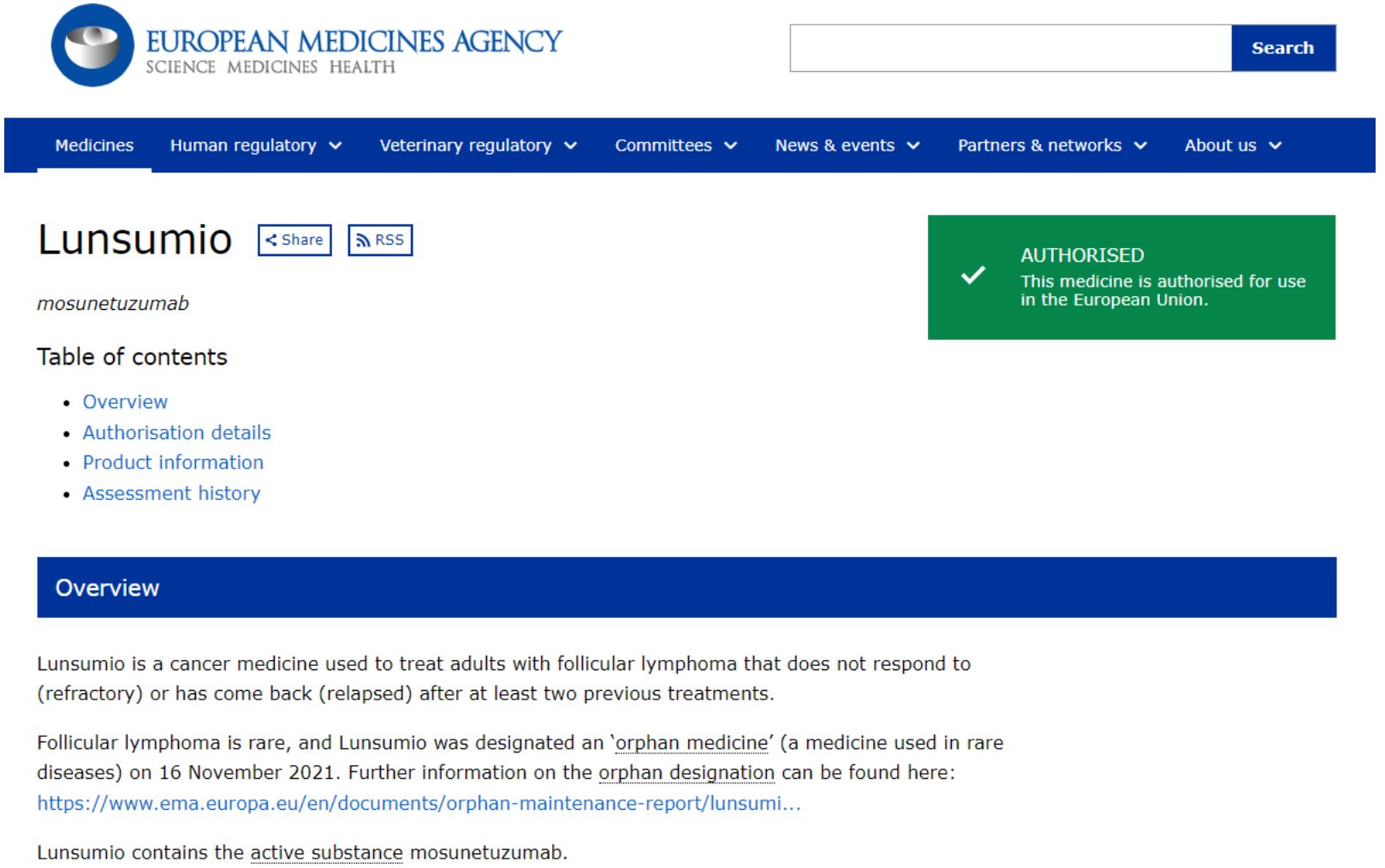
Hutchings M, *et al. Lancet* 2021; 398(10306): 1157-1169.

Activity against FL in the phase 1 studies of CD3/CD20 BsABs - overview

Molecule	ORR	CRR	CRS	CRS gr. 3-4
Mosunetuzumab	66%	35%	27%	1%
Odronextamab	91%	72%	61%	7%
Glofitamab	79%	71%	67%	5%
Epcoritamab	90%	50%	66%	0%

Recent data from the phase 2 study of mosunetuzumab in r/r FL

First in class and first to the market


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Search

Medicines | Human regulatory | Veterinary regulatory | Committees | News & events | Partners & networks | About us

Lunsumio Share RSS

mosunetuzumab

AUTHORISED
This medicine is authorised for use in the European Union.

Table of contents

- Overview
- Authorisation details
- Product information
- Assessment history

Overview

Lunsumio is a cancer medicine used to treat adults with follicular lymphoma that does not respond to (refractory) or has come back (relapsed) after at least two previous treatments.

Follicular lymphoma is rare, and Lunsumio was designated an 'orphan medicine' (a medicine used in rare diseases) on 16 November 2021. Further information on the orphan designation can be found here: https://www.ema.europa.eu/en/documents/orphan-maintenance-report/lunsumi...

Lunsumio contains the active substance mosunetuzumab.

https://www.ema.europa.eu/en/medicines/human/EPAR/lunsumio. Approved 23 June 2022

Phase 2 study of mosunetuzumab in r/r FL - overview

- 90 patients included (at 49 centres!)
- Median follow-up 18.3 months
- No mandatory hospitalisation
- All patients were aged 18 years or older
- histologically confirmed follicular lymphoma (grade 1–3a)
- ECOG performance status of 0–1
- R/R to ≥ 2 previous lines of treatment, including
  - an anti-CD20 therapy
  - an alkylating agent
- Treated to a maximum of 17 cycles
- Re-treatment was allowed in complete responders who progressed after completion of initial treatment.

Treatment schedule:

- 21-day cycles
- Cycle 1 step-up dosing:
  - 1 mg on cycle 1 day 1
  - 2 mg on cycle 1 day 8
  - 60 mg on cycle 1 day 15
- 60 mg on cycle 2 day 1
- 30 mg on day 1 of subsequent cycles

Budde LE, et al. Lancet Oncol 2022; 23: 1055–65

Phase 2 study of mosunetuzumab in r/r FL - patients

Median age 60 years

Ann Arbor stage

- I 5 (6%)
- II 16 (18%)
- III 25 (28%)
- IV 44 (49%)

- Previous autologous stem cell transplant: 19 (21%)
- Refractory to last previous therapy: 62 (69%)
- Refractory to any previous anti-CD20 therapy: 71 (79%)
- Double refractory (alkylator + CD20): 48 (53%)
- POD24: 47 (52%)

Number of previous lines of therapy: 3 (2–4)

- Two previous lines 34 (38%)
- Three previous lines 28 (31%)
- < 3 previous lines 28 (31%)

Budde LE, et al. Lancet Oncol 2022; 23: 1055–65

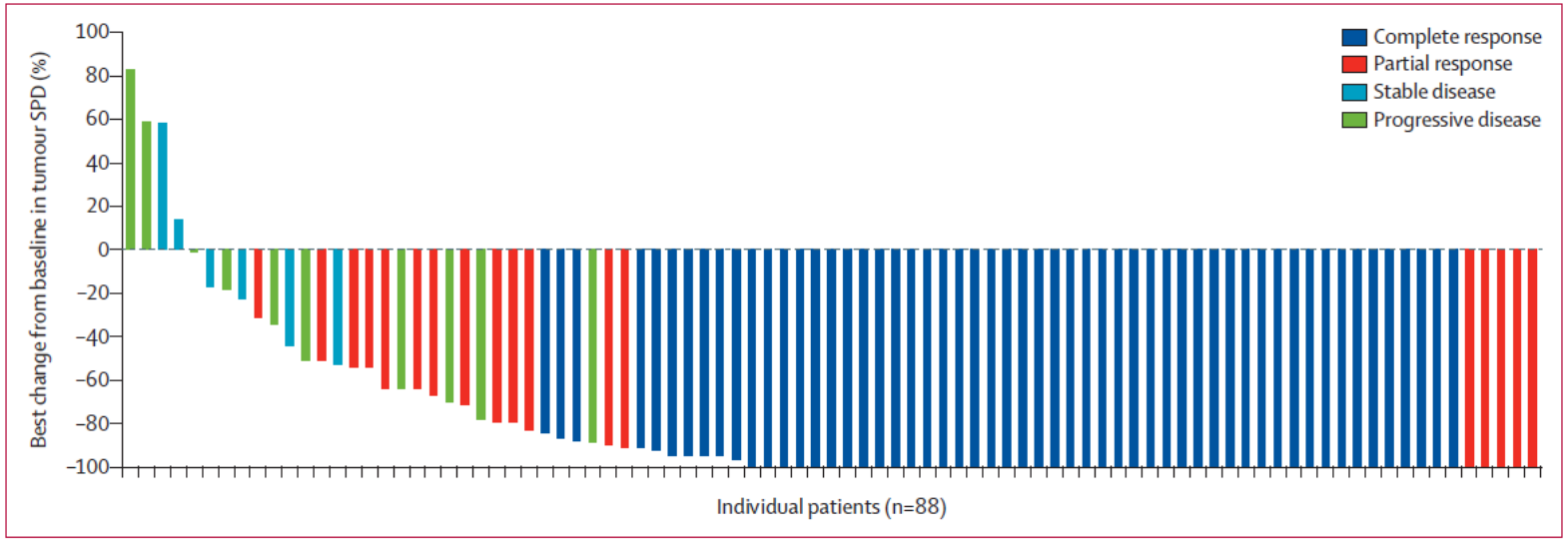
Phase 2 study of mosunetuzumab in r/r FL – selected AEs

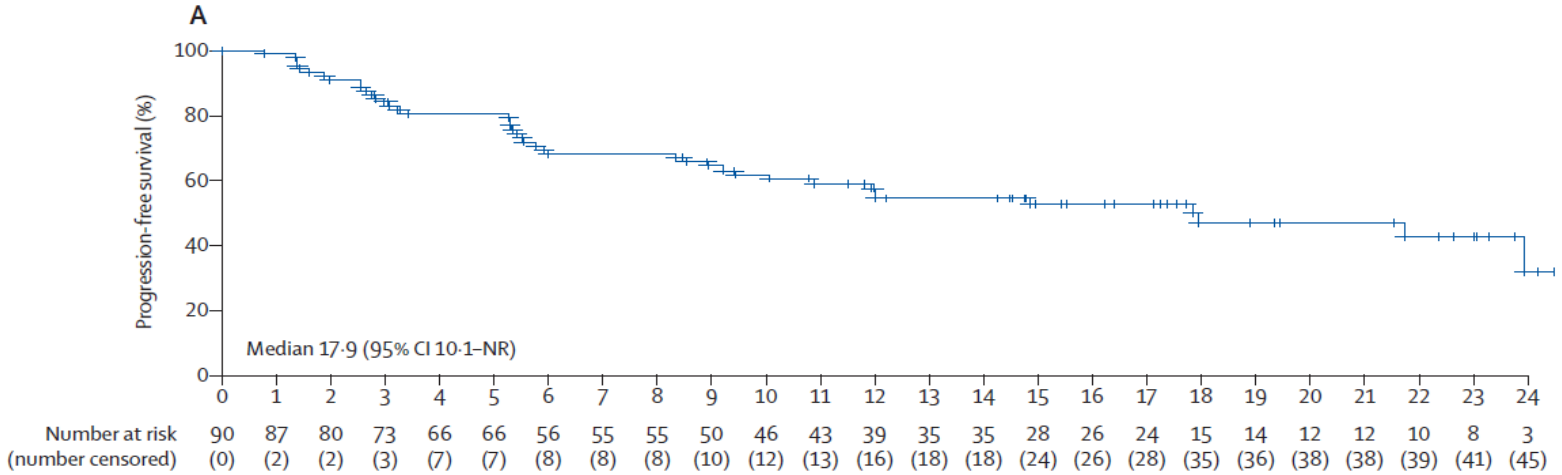
	Grade 1-2	Grade 3	Grade 4
Cytokine release syndrome	38 (42%)	1 (1%)	1 (1%)
Fatigue	33 (37%)	0	0
Neutropenia	2 (2%)	12 (13%)	12 (13%)
Hypohosphatemia	9 (10%)	15 (17%)	0
Hypokalemia	15 (17%)	2 (2%)	0
Thrombocytopenia	5 (6%)	0	4 (4%)
Anemia	5 (6%)	7 (8%)	0
Increased ALT	6 (7%)	4 (4%)	1 (1%)
Abdominal pain	8 (9%)	1 (1%)	0
Back pain	8 (9%)	1 (1%)	0
Urinary tract infection	8 (9%)	1 (1%)	0

*AEs only occuring in grade 1 not included in the table

Budde LE, et al. Lancet Oncol 2022; 23: 1055–65

Phase 2 study of mosunetuzumab in r/r FL - efficacy





- ORR 72%
- CR rate: 54%
- Median DoR: 22.8 mo
- Median DoCR: NR
- Median PFS 17.9 mo

Budde LE, et al. Lancet Oncol 2022; 23: 1055–65

Mosunetuzumab update at EHA 2022
Comparison of patients ≥65 and <65 years

Response rates and DoR

Efficacy endpoint	<65 years (N=60)	≥65 years (N=30)
CR rate, % (95% CI)	55.0 (41.6–67.9)	70.0 (50.6–85.3)
ORR, % (95% CI)	76.7 (64.0–86.6)	86.7 (69.3–96.2)
DoR		
Median, months (95% CI)	22.8 (8.7–NE)	18.7 (9.4–NE)
18-month event-free rate, % (95% CI)	58.5 (43.3–73.8)	53.5 (30.8–76.3)
DoCR		
Median, months (95% CI)	NE (9.1–NE)	18.7 (13.7–NE)
18-month event-free rate, % (95% CI)	66.6 (48.0–85.2)	61.7 (36.2–87.2)

CRS events

CRS event	<65 years (N=60)	≥65 years (N=30)
Patients with a CRS event, n (%)	31 (52)	9 (30)
CRS Grade, n (%)		
Grade 1	17 (28)	6 (20)
Grade 2	13 (22)	2 (7)
Grade 3	0	1 (3)
Grade 4	1 (2)	0
Median duration of CRS events, days (range)	3 (1–29)	3 (1–8)
Management approach, n/N (%)		
Tocilizumab	5/31 (16)	2/9 (22)
Corticosteroids	7/31 (23)	3/9 (33)

Matthew Matasar, et al. Presented at EHA 2022; No. P1126

Mosunetuzumab update at EHA 2022
Comparison of patients ≥65 and <65 years

Key Results (N=90)

- Compared with younger pts, those aged ≥65 yr had a numerically higher ORR (87% vs 77%) and CR rate (70% vs 55%)
- 18-month DOR: 54% (95% CI: 31–76) in ≥65 yr and 59% (95% CI: 43–74) in <65 yr
- Gr 3-4 AEs: 73% vs 68% in pts ≥65 yr vs <65 yr
- SAEs of any Gr: 37% vs 52% in ≥65 yr vs <65 yr
- One pt in each age group discontinued due to mosunetuzumab-related AEs
- CRS: 30% vs 52% in ≥65 yr vs <65 yr (All CRS events resolved)

Conclusions

- Mosunetuzumab is efficacious with low rates of severe CRS events and no drug-related fatal AEs in older and younger pts with R/R FL who have received ≥ 2 prior therapies
- The safety profile of mosunetumab is generally similar between old and younger pts, but numerically lower rates of CRS events and SAEs were observed in older pts

Matthew Matasar, et al. Presented at EHA 2022; No. P1126

Combination studies of bispecifics in r/r FL

Epcoritamab with rituximab + lenalidomide in R/R FL

Baseline Demographics

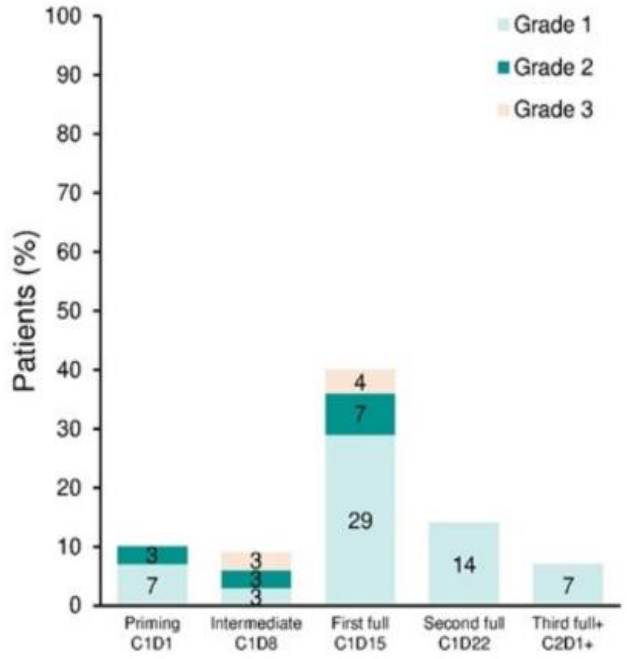
Characteristic	Arm 2a N=30	Arm 2b N=44
Median age, y (range)	68 (42–80)	66 (30–79)
Female, n (%)	17 (57)	22 (50)
Ann Arbor stage, n (%)[a]		
II	3 (10)	2 (5)
III	6 (20)	14 (32)
IV	21 (70)	27 (61)
Histologic grade, n (%)[b]		
1	4 (13)	3 (7)
2	20 (67)	21 (48)
3A	5 (17)	14 (32)
FLIPI, n (%)[c]		
0–1	2 (7)	1 (2)
2	8 (27)	11 (25)
3–5	20 (67)	20 (45)
Median time from diagnosis to first dose, mo (range)	89 (6–281)	73 (4–331)
Median number of prior lines of therapy (range)	1 (1–5)	2 (1–9)
1 prior line, n (%)	18 (60)	20 (45)
2 prior lines, n (%)	5 (17)	13 (30)
≥3 prior lines, n (%)	7 (23)	9 (20)
Primary refractory disease, n (%)[d]	9 (30)	12 (27)
Progressed within 24 mo of initial therapy, n (%)	12 (40)	19 (43)
Refractory to last line of therapy, n (%)[d]	8 (27)	12 (27)
Median time from end of last line of therapy to first dose, mo (range)	31 (1–213)	17 (2–198)

CRS profile:

CRS Graded by Lee et al 2019 Criteria in Arm 2a

	Arm 2a N=30
CRS, n (%)	15 (50)
Grade 1	9 (30)
Grade 2	4 (13)
Grade 3	2 (7)
CRS resolution, n (%)	15 (100)
Median time to resolution, d (range)[a]	4 (1–15)
CRS leading to treatment discontinuation, n (%)	1 (3)
Tocilizumab use, n (%)	3 (10)

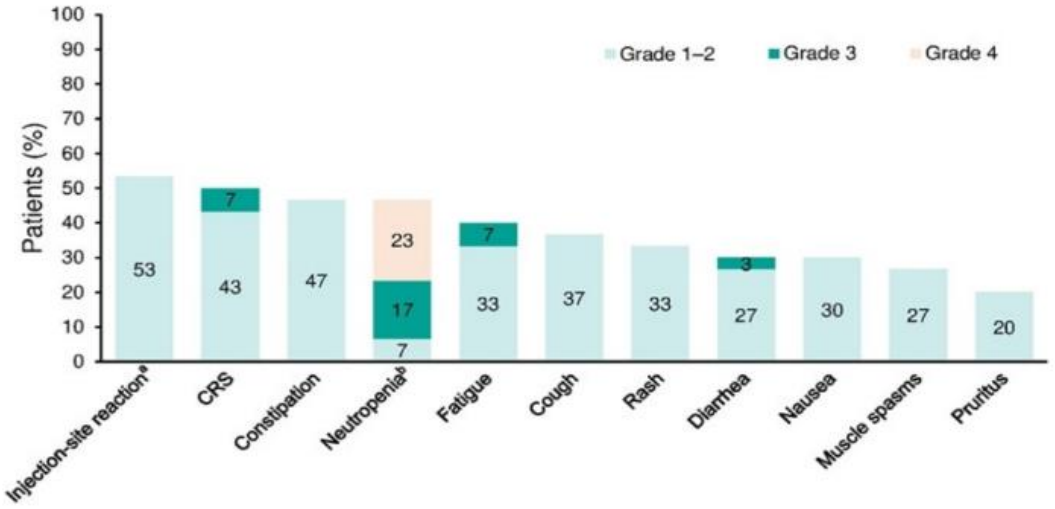
CRS Events by Dosing Period in Arm 2a



David Belada et al. Presented at ASCO 2022; No. P1135

Epcoritamab with rituximab + lenalidomide in R/R FL

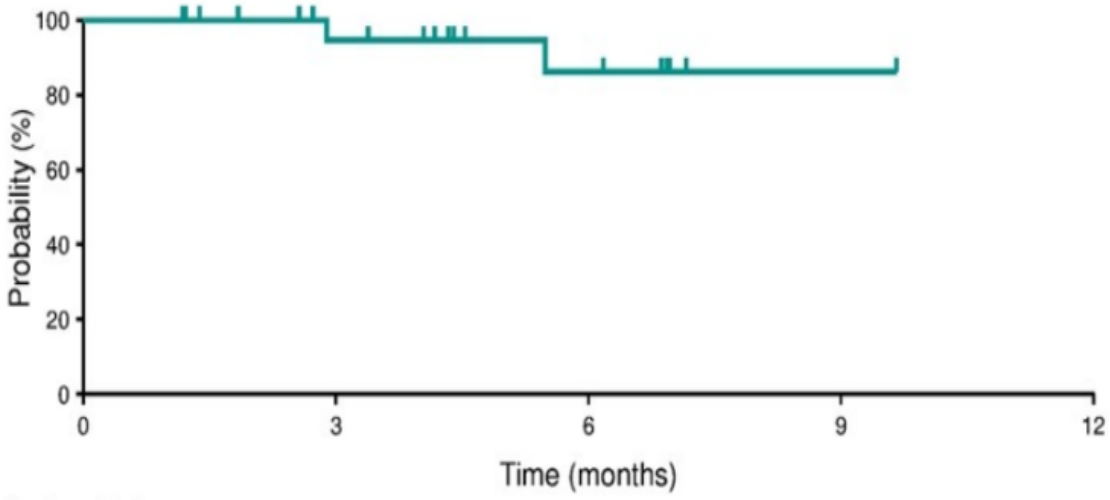
Treatment-Emergent AEs (≥20%) by Grade in Arm 2a



Best Overall Responses at Any Time and at 6 Weeks

Response, n (%)[a]	At any time Arm 2a n=28[b]	At 6 weeks Arm 2a n=27	At 6 weeks Arm 2b n=28
Overall response	28 (100)	25 (93)	26 (93)
CMR	27 (96)	19 (70)	17 (61)
PMR	1 (4)	6 (22)	9 (32)
Stable disease	0	2 (7)	1 (4)
Progressive disease	0	0	1 (4)

Duration of Response for Arm 2a (48 mg)



David Belada et al. Presented at ASCO 2022; No. P1135

Epcoritamab with rituximab + lenalidomide in R/R FL

Key Results (Arm 2a, N=30)

- At a median FU of 5.1 mo (0.8–12.3), 25 pts (83%) remained on Tx
- ORR 100%; CMR 96% (arm 2a)
- All responders remained in response
- Longest DOR 7.0+ mo and ongoing
- 5 pts discontinued due to PD (n=2), AEs (n=2), or consent withdrawal (n=1)
- CRS in 15 pts (50%; G1/2 43%, G3 7%)
- All CRS events resolved
- 1 pt discontinued due to CRS
- 1 pt experienced G2 ICANS.
- No fatal TEAEs

Conclusions

- Epcoritamab + R^2 showed encouraging responses, with all pts in arm 2a achieving a response
- Based on response rates at week 6, pts in arm 2b showed similarly encouraging efficacy
- Epcoritamab + R^2 demonstrated a manageable safety profile – mainly low-grade CRS (all resolved) and one ICANS event (grade 2, resolved)
- These updated data support further exploration of Epcoritamab + R^2 in pts with R/R FL

David Belada et al. Presented at ASCO 2022; No. P1135

Conclusions

- The CD3/CD20 bispecific antibodies show very high antitumor activity in r/r FL and manageable toxicity:

Molecule	ORR	CRR	CRS	CRS gr. 3-4
Mosunetuzumab	66%	35%	27%	1%
Odronextamab	91%	72%	61%	7%
Glofitamab	79%	71%	67%	5%
Epcoritamab	90%	50%	66%	0%

- Mosunetuzumab in phase 2:
  - 72% ORR, 54% CRR
  - Many responses durable and median PFS 18 months
- Mosunetuzumab is approved for the treatment of r/r FL in 3+ line
- A number of combination studies are ongoing or planned for FL:
  - Lenalidomide and newer CelMods, Polatuzumab vedotin

Thank you