Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

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Expert:innen berichten zu Lymphomen & Leukämien

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San Diego & virtuell

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Prof. Dr. med. Peter Borchmann
Uniklinik Köln

Diffuses großzelliges B-Zell-Lymphom (DLBCL)

Disclosures

Employment, management position	–
Advisory/expert activity	Takeda, BMS, Roche, Amgen, Novartis, Celgene, Miltenyi Biotech, Gilead
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Intangible conflicts of interest	–

Kapitel 1

Bispezifische Antikörper: Wie sehen die Daten mit längerem FU aus? Gibt es Risikofaktoren?

Glofitamab Monotherapy in Relapsed or Refractory Large B-Cell Lymphoma: Extended Follow-Up from a Pivotal Phase II Study and Subgroup Analyses in Patients with Prior Chimeric Antigen Receptor T-Cell Therapy and by Baseline Total Metabolic Tumor Volume

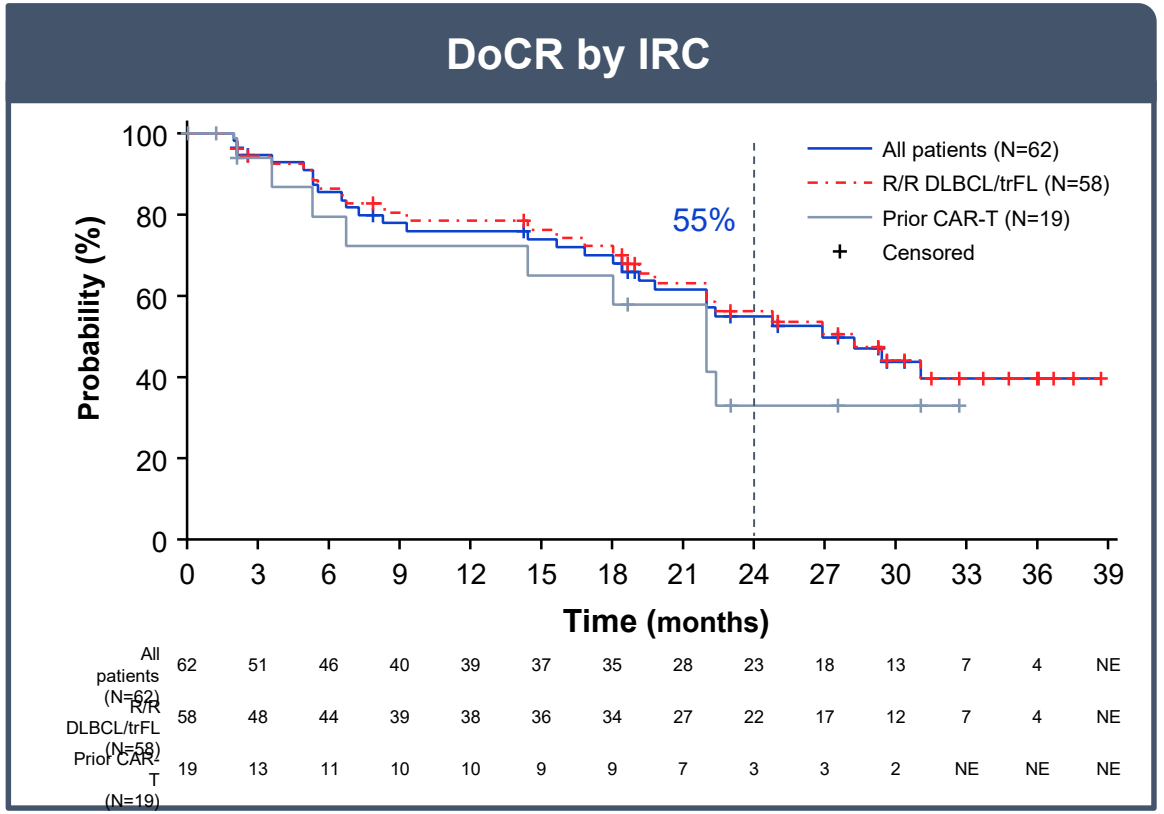
Martin Hutchings et al., Abs 433

n (%)*		All patients (N=154)†
Median age, years (range)		66.0 (21–90)
Male		100 (64.9)
ECOG PS‡	0	69 (44.8)
	1	84 (54.5)
Ann Arbor stage	I/II	35 (22.7)
	III/IV	116 (75.3)
NHL subtype	DLBCL	110 (71.4)
	trFL	28 (18.2)
	HGBCL	10 (6.5)
	PMBCL	6 (3.9)
Bulky disease	>6cm	64 (41.6)
	>10cm	19 (12.3)

n (%)*	All patients (N=154)†
Median no. of prior lines, n (range)	3 (2–7)
2 prior lines	61 (39.6)
≥3 prior lines	93 (60.4)
Prior CAR-T	51 (33.1)
Refractory to prior CAR-T§	46 (29.9)
Prior ASCT	29 (18.8)
Refractory to any prior therapy	138 (89.6)
Refractory to last prior therapy	131 (85.1)
Refractory to first line of prior therapy	90 (58.4)
Refractory to any prior anti-CD20	128 (83.1)

Response rates and DoCR

	All patients (N=155)*	R/R DLBCL/ trFL (N=132)[1†‡]	Prior CAR-T (N=52)[†]
ORR, n (%) [95% CI]	80 (52) [43.5–59.7]	74 (56) [47.2–64.7]	26 (50) [35.8–64.2]
CR rate, n (%) [95% CI]	62 (40) [32.2–48.2]	58 (44) [35.3–52.8]	19 (37) [23.6–51.0]
Median DoCR, months (95% CI)	26.9 (19.8–NR)	28.3 (19.8–NR)	22.0 (6.7–NR)
24-month DoCR, % (95% CI)	55.0 (41.1–68.8)	56.2 (41.9–70.4)	33.1 (7.2–59.0)
Median CR follow-up, months (range)	29.6 (0–39)	29.6 (0–39)	23.0 (0–33)
Ongoing CRs, n/N (%)	34/62 (55)	32/58 (55)	10/19 (53)



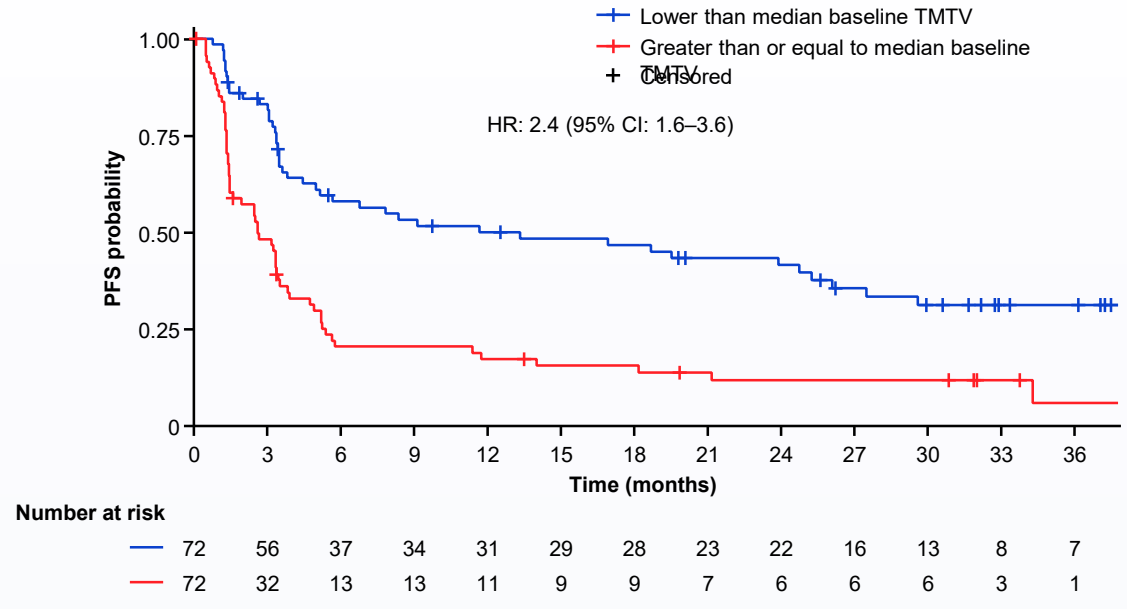
- Median time on study: 32.1 months (range: 0–43)

Association between baseline TMTV and PFS

- Baseline TMTV was derived from baseline PET images using a semi-automated method with a threshold for TMTV of 2x the SUV_{mean} of the liver
- Median baseline TMTV was 128.7mL (range: 0–3820; n=144*)

	Baseline TMTV ≥ median (n=72)	Baseline TMTV < median (n=72)
24-month PFS rate, % (95% CI)	11.8 (6.0–23.5)	41.6 (31.1–55.6)

PFS by TMTV at baseline



Safety summary

*By ASTCT grade. AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy criteria; ICANS, immune effector cell-associated neurotoxicity syndrome; SAE, serious adverse event.

- **CRS* remained the most common AE**
  - CRS occurred in 64% of patients
  - CRS events were mostly Grade 1 (48%) or Grade 2 (12%); Grade 3 (3%) and Grade 4 (1%) events were uncommon
- **The incidence of AEs and SAEs was stable compared with earlier analyses[1,2]**
  - No new AEs were reported, including ICANS, CRS, infections, or Grade 5 AEs

N (%)	N=154
AE Glofitamab-related	152 (99) 140 (91)
Grade ≥3 AE Glofitamab-related	100 (65) 69 (45)
SAE Glofitamab-related	75 (49) 46 (30)
Grade 5 (fatal) AE Glofitamab-related	11 (7) 0
AE leading to treatment discontinuation Glofitamab-related	14 (9) 5 (3)
AE leading to dose modification/interruption of glofitamab Glofitamab-related	29 (19) 16 (10)

1
2

The safety profile was consistent with previous analyses, with no new AEs reported[1,2]

Zusammenfassung

- Längeres FU (32m) mit Glofitamab zeigt auch bei CR PatientInnen kein Plateau
- Tumorvolumen scheint ein relevanter Faktor für das PFS zu sein
- Keine neuen Sicherheitssignale

Kapitel 2

Wie sieht es mit CARs bei älteren PatientInnen aus?

1761 Improved Overall Survival With Axicabtagene Ciloleucel vs Standard of Care in Second-Line Large B-Cell Lymphoma Among the Elderly: A Subgroup Analysis of ZUMA-7. MJ Kersten, *Netherlands*

DLBCL 2nd line| Pat Charakteristika

Table 1. Baseline Patient and Disease Characteristics Among Elderly Patients

Characteristic	Axi-Cel, ≥65 Years N=51	SOC, ≥65 Years N=58	Overall, ≥65 Years N=109
Median age, years (range)	70 (65-80)	69 (65-81)	69 (65-81)
Sex, male, n (%)	28 (55)	39 (67)	67 (61)
Disease stage III-IV, n (%)	42 (82)	44 (76)	86 (79)
Derived sAAIPI total score of 2, n (%)	27 (53)	18 (31)	45 (41)
Response to 1L therapy,[a] n (%)			
Primary refractory	37 (73)	39 (67)	76 (70)
Relapse ≤12 months of 1L therapy	14 (27)	19 (33)	33 (30)
Disease type per investigator, n (%)			
DLBCL not specified	27 (53)	40 (69)	67 (61)
T-cell/histiocyte-rich LBCL	0 (0)	1 (2)	1 (1)
Large cell transformation from follicular lymphoma	7 (14)	9 (16)	16 (15)
HGBL with or without *MYC* and *BCL2* and/or *BCL6* rearrangement	17 (33)	8 (14)	25 (23)
Elevated LDH[b] level	31 (61)	24 (41)	55 (50)

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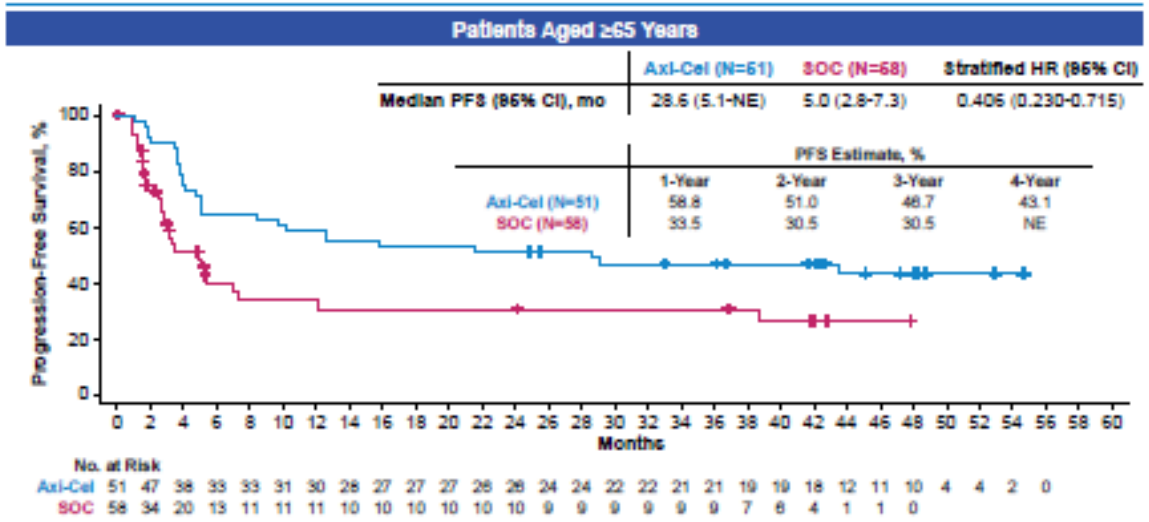
DLBCL 2nd line| Safety Outcomes

	Axi-Cel, ≥65 Years N=49		SOC, ≥65 Years N=55	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
AEs of Interest, n (%)				
CRS	48 (98)	4 (8)	–	–
Neurologic event	33 (67)	13 (27)	14 (25)	1 (2)
Hypogammaglobulinemia	10 (20)	0 (0)	1 (2)	0 (0)
Cytopenia	41 (84)	41 (84)	45 (82)	42 (76)
Infections	30 (61)	14 (29)	21 (38)	9 (16)
Reason for Death, n (%)	25 (51)		29 (53)	
Progressive disease	20 (41)		20 (36)	
Grade 5 AE during protocol-specific reporting period	2 (4)[a]		1 (2)[b]	
New or secondary malignancy	1 (2)[c]		0 (0)	
Other reason for death	2 (4)[d]		8 (15)[e]	
Definitive therapy–related mortality	0 (0)		1 (2)[f]	

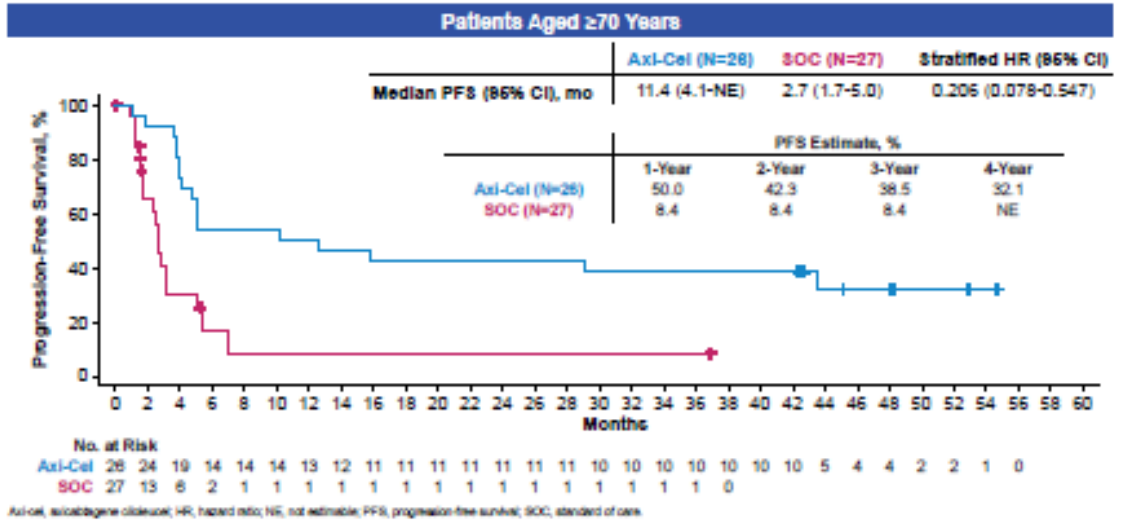
1761 Improved Overall Survival With Axicabtagene Ciloleucel vs Standard of Care in Second-Line Large B-Cell Lymphoma Among the Elderly: A Subgroup Analysis of ZUMA-7. MJ Kersten, *Netherlands*

DLBCL 2nd line| Efficacy Outcomes

PFS Axi cel vs SOC > 65 Jahre



PFS Axi cel vs SOC > 70 Jahre



Zusammenfassung

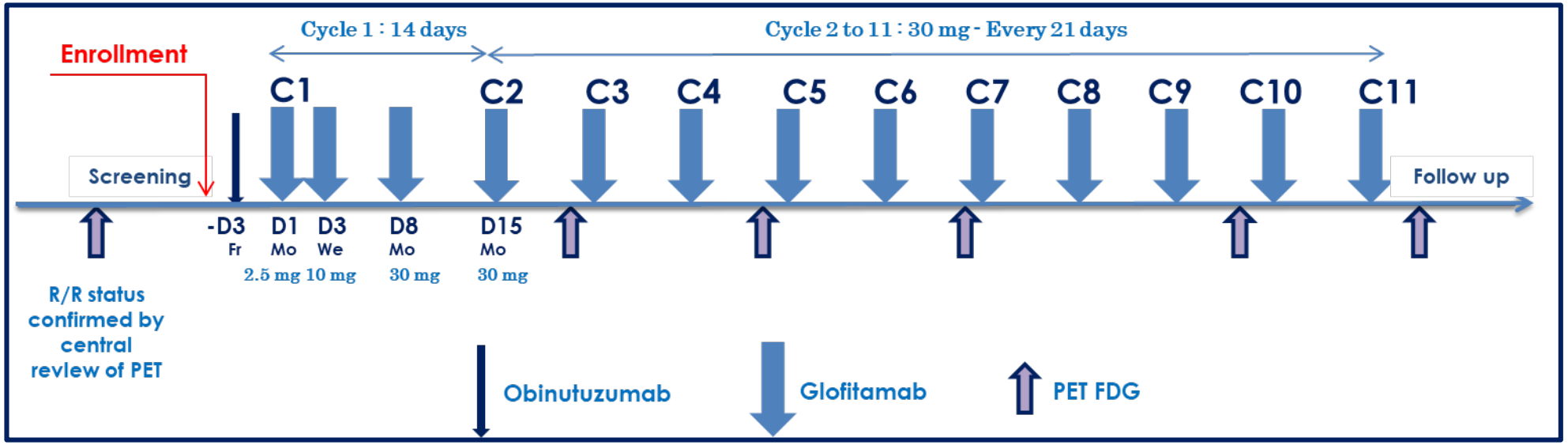
- Axi-cel zeigt auch bei den älteren PatientInnen (70 Jahre im Median) einen deutlichen PFS Vorteil
- Und war hinsichtlich der Sicherheit nicht anders als bei der Gesamtkohorte in ZUMA-7 beobachtet
- Authors´conclusion: Alter allein sollte kein Ausschluss für HR-2nd line PatientInnen mit R/R LBCL sein

Kapitel 3

Wie sieht die Sequenz von CARs und Bispecs aus?

Abs 893 Glofitamab Monotherapy in Patients with non-Hodgkin B-cell Lymphoma after Failing CAR T-cell Infusion
Primary Analysis of the BiCAR study, a phase II LYSA study. Sesque et al.

Glofitamab IV administration according to BiCAR study



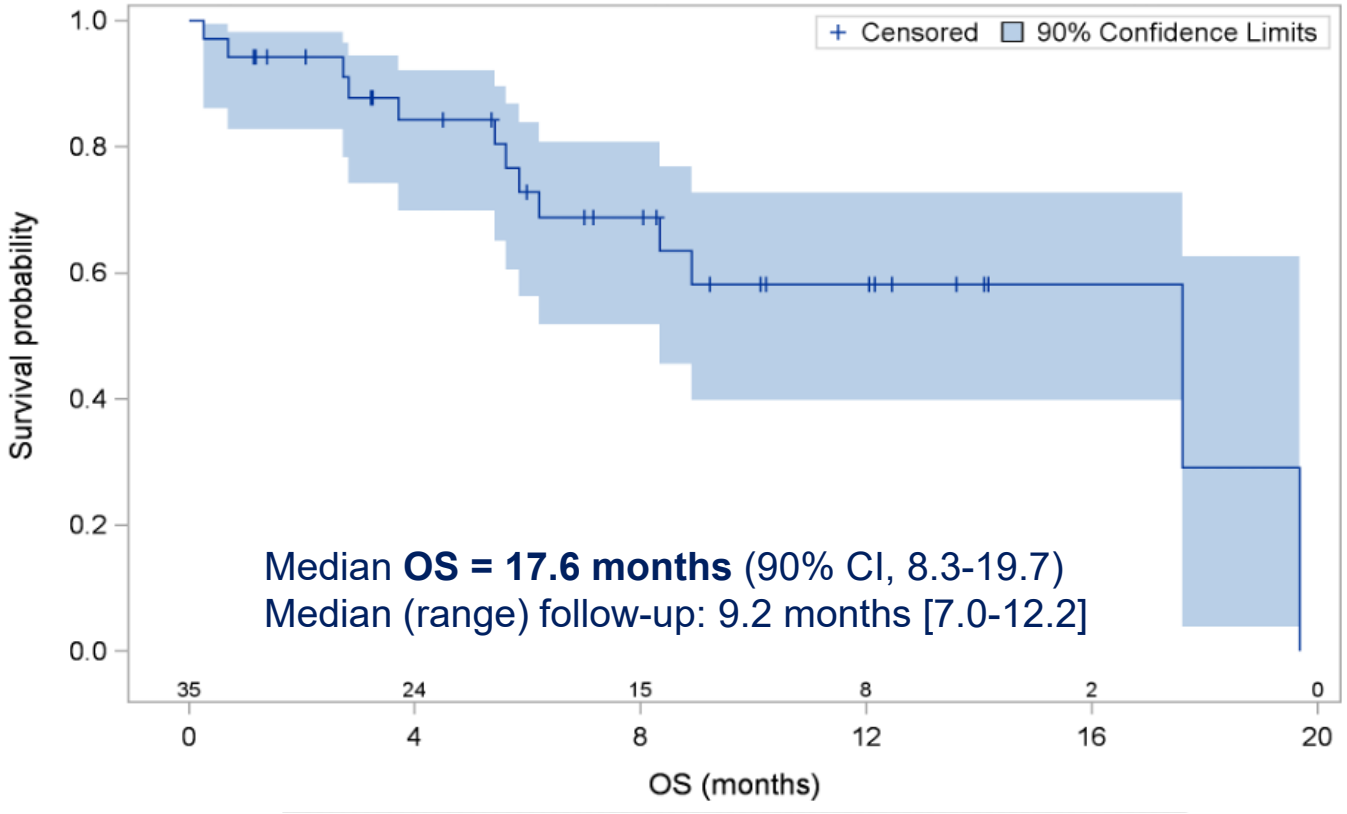
BiCAR Patients' characteristics

	Cohort 1 N=44	Cohort 2 N=19	FAS N=63
Male, N (%)	30 (68.2)	12 (63.2)	42 (66.7)
Median Age, yrs (range)	64.5 (33-77)	66 (42-76)	**65** (33-77)
ECOG 0-1, N (%)	44 (100)	19 (100)	63 (100)
Ann Arbor Stage III/IV, N (%)	37 (84.1)	16 (84.2)	53 (84.1)
IPI ≥ 3, N (%)	26 (59)	11 (57.8)	37 (58.7)
NHL subtypes*, N (%) DLBCL FL MCL t-FL Others histologies*	44 (100)	- 6 (31.5) 5 (26.3) 4 (21) 4 (21)	44 (69.8) 6 (9.5) 5 (7.9) 4 (6.3) 4 (6.3)
Median number of previous lines, N (range)	3 (2-5)	3 (3-6)	**3** (2-6)
Number of patients ≥ 3 lines of treatment, N (%)	36 (81.8)	19 (100)	55 (87.3)
CAR T-cell, N (%) Axi-Cel Tisa-Cel Brexu-Cel Exp. Product	24 (54.5) 17 (38.6) - 3 (6.8)	5 (26.3) 8 (42.1) 5 (26.3) 1 (5.3)	29 (46) 25 (39.7) 5 (7.9) 4 (6.3)
Refractory to CAR T-cells (NMR/PD), N (%)	12 (27.3)	1 (5.3)	13 (**20.6**)
Relapse/progression after CAR T-cells, N (%) 1-3 mo 3-6 mo > 6 mo	32 (72.7) 9 (28.1) 8 (25) 15 (46.9)	18 (94.7) 6 (33.3) 10 (55.6) 2 (11.1)	50 (79.4) 15 (**30**) 18 (**36**) 17 (34)

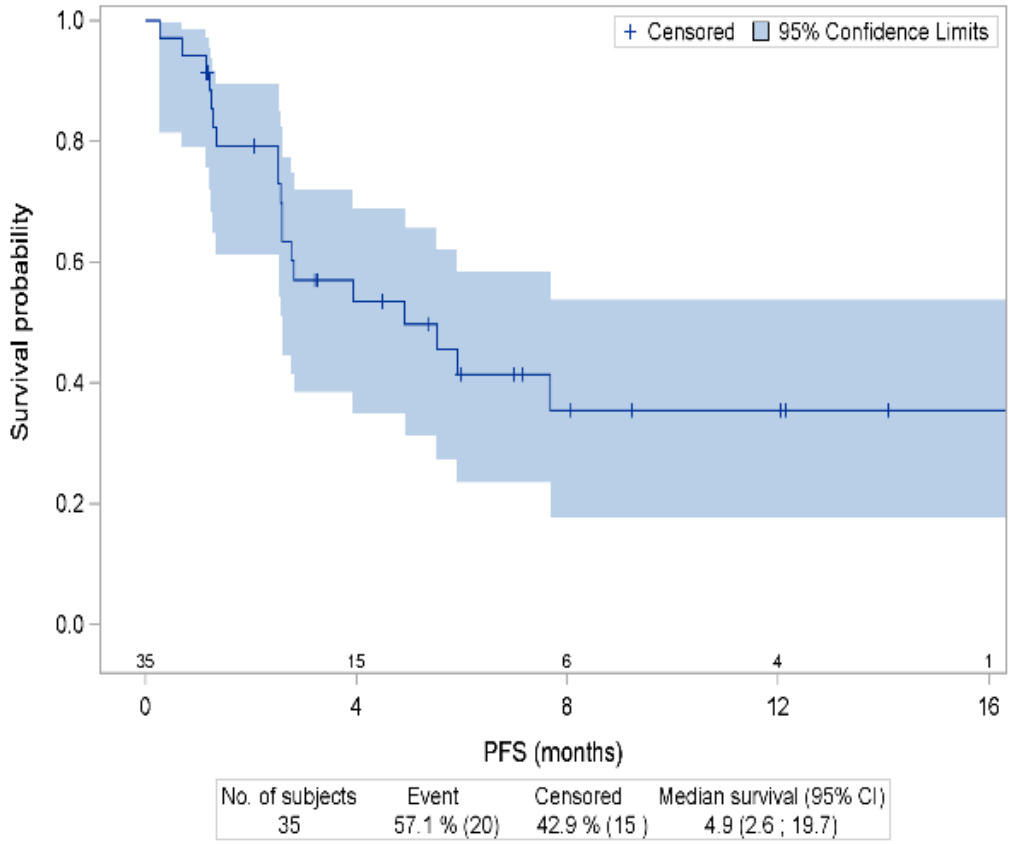
*Each histological diagnosis was confirmed by biopsy before the inclusion of all patients included in cohort 1.
For patients with multiple histologies, the diagnostic indicated corresponds to the result of the last biopsy performed. DLBCL, FL, MCL, MZL, t-MW

Primary Endpoint Overall Survival for Patients in Cohort 1

Primary Endpoint was met
mOS : 17.6 mo vs 12.6 mo (H1)



Sec Endpoint PFS, med. 4.9 m



Conclusions

- Es wurde in dieser schwierigen Situation durchaus gutes Ansprechen beobachtet (ORR = 67 % / CR = 36.4%)
- Das mediane Gesamtüberleben war länger als geschätzt und erforderlich zur Erreichung des primären Endpunkts (17.6 m)
- Bestätigt die Beobachtung aus der pivotalen Phase II Studie, dass die Therapie mit bispezifischen AK nach CAR T-Zelltherapie Versagen sinnvoll ist

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2023

Für den Inhalt verantwortlich:

Prof. Dr. med. Peter Borchmann

Uniklinik Köln

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

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