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DLBCL: status quo 2021

Peter Borchmann

C-LWG

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Offenlegung potentieller Interessenskonflikte

Employment, management position	–
Advisory/expert activity	Takeda, BMS, Roche, Amgen, Novartis, Celgene, Miltenyi Biotech, Gilead
Ownership (shares, stocks, funds)	–
Patent, copyright, sales license	–
Honoraria	Takeda, Novartis, BMS, Roche, MSD, Celgene, Miltenyi Biotech, Gilead, Abbvie
Funding scientific research	Takeda Oncology, MSD, Novartis
Other financial relationships	–
Intangible conflicts of interest	–

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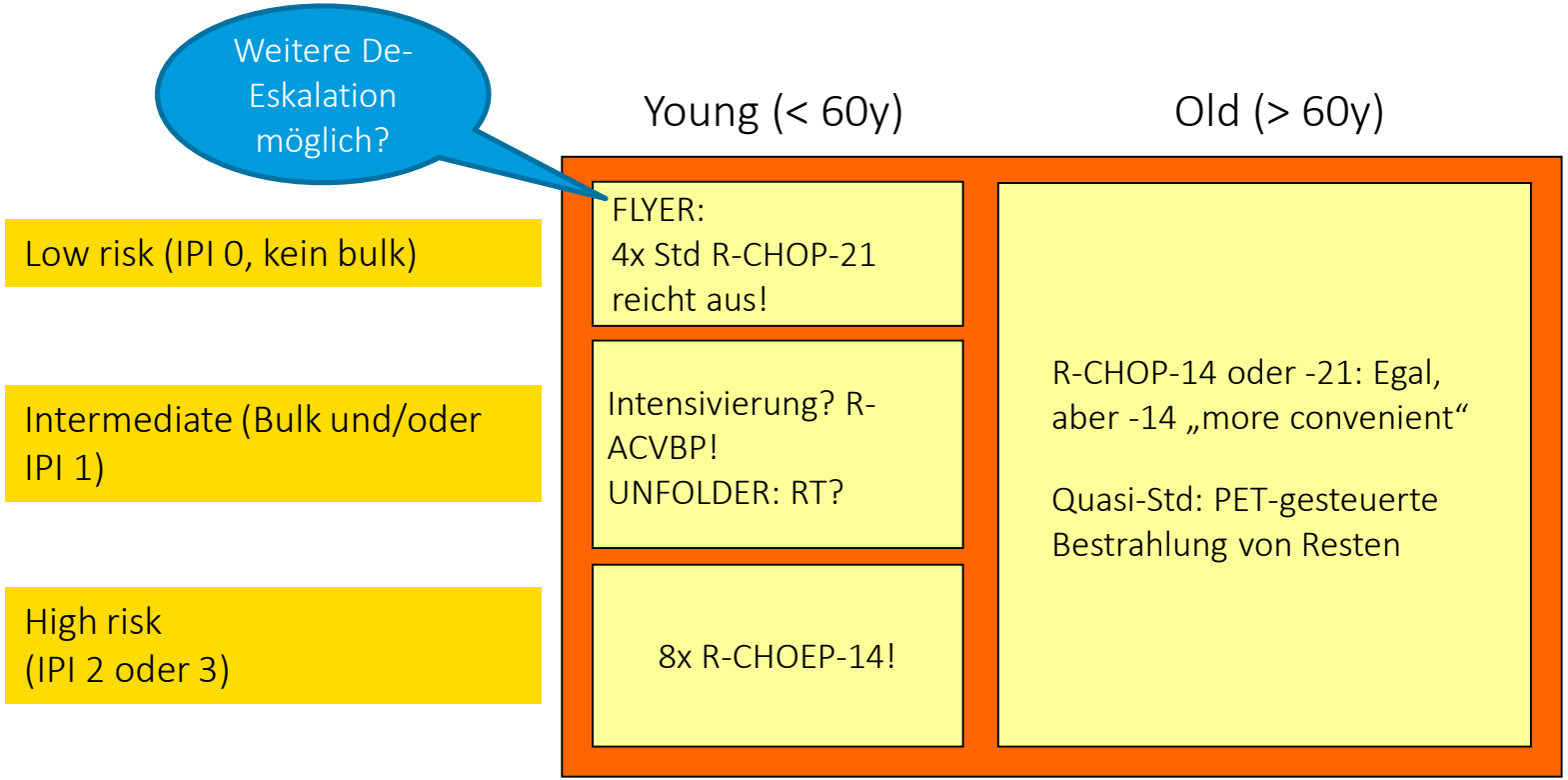
DLBCL: status quo 2021

1. First line

2. Later lines: revival of Immunotherapy
   - Naked CD19 antibody (plus lenalidomide)
   - antibody drug conjugates
   - CD3xCD20 bispecific antibodies
   - CD19 targeting CAR T-cell therapies

3. Summary and perspectives

Erstlinien-Therapie des DLBCL: Zusammenfassung der DSHNHL Sicht



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EARLY POSITRON EMISSION TOMOGRAPHY RESPONSE-ADAPTED TREATMENT IN LOCALIZED DIFFUSE LARGE B-CELL LYMPHOMA (AAIPI=0) : RESULTS OF THE PHASE 3 LYSA LNH 09-1B TRIAL: Bologna et al. ICML 2021

Background

R-CHOP 21 = standard treatment of diffuse large B-cell lymphoma (DLBCL)

- Based on previous studies in past NHL programs
- 6 cycles without radiation therapy is the reference in localized disease for LYSA

2019 : FLYER trial

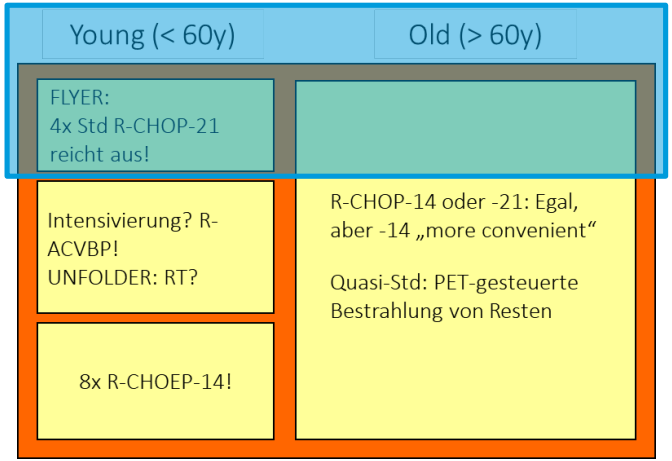
- 4 cycles of R-CHOP 21 could be as effective as 6 cycles in the younger population

  (Poeschel et al., Lancet, 2019)

Early TEP response to drive treatment strategy

- Early positron emission tomography (ePET) is effective to drive treatment for patients with DLBCL and aaIPI score ≥ 1

  (Casasnovas et al., Blood, 2017)



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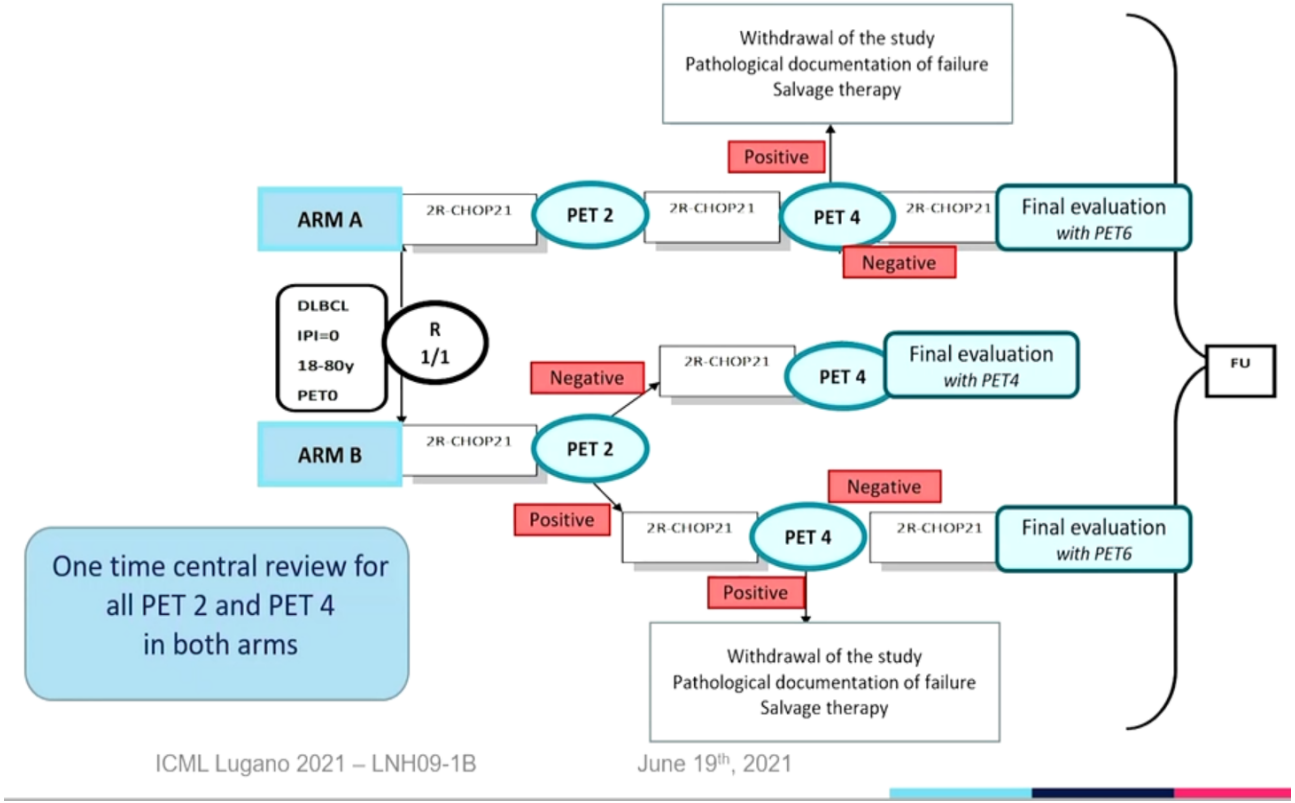
PET-RESPONSE-ADAPTED TREATMENT IN LOCALIZED DIFFUSE LARGE B-CELL LYMPHOMA: PHASE 3 LYSA LNH 09-1B TRIAL



- Arms well balanced
- ~ 45% > 60 years
- ~ 60% male
- ~ 50% extranodal sites

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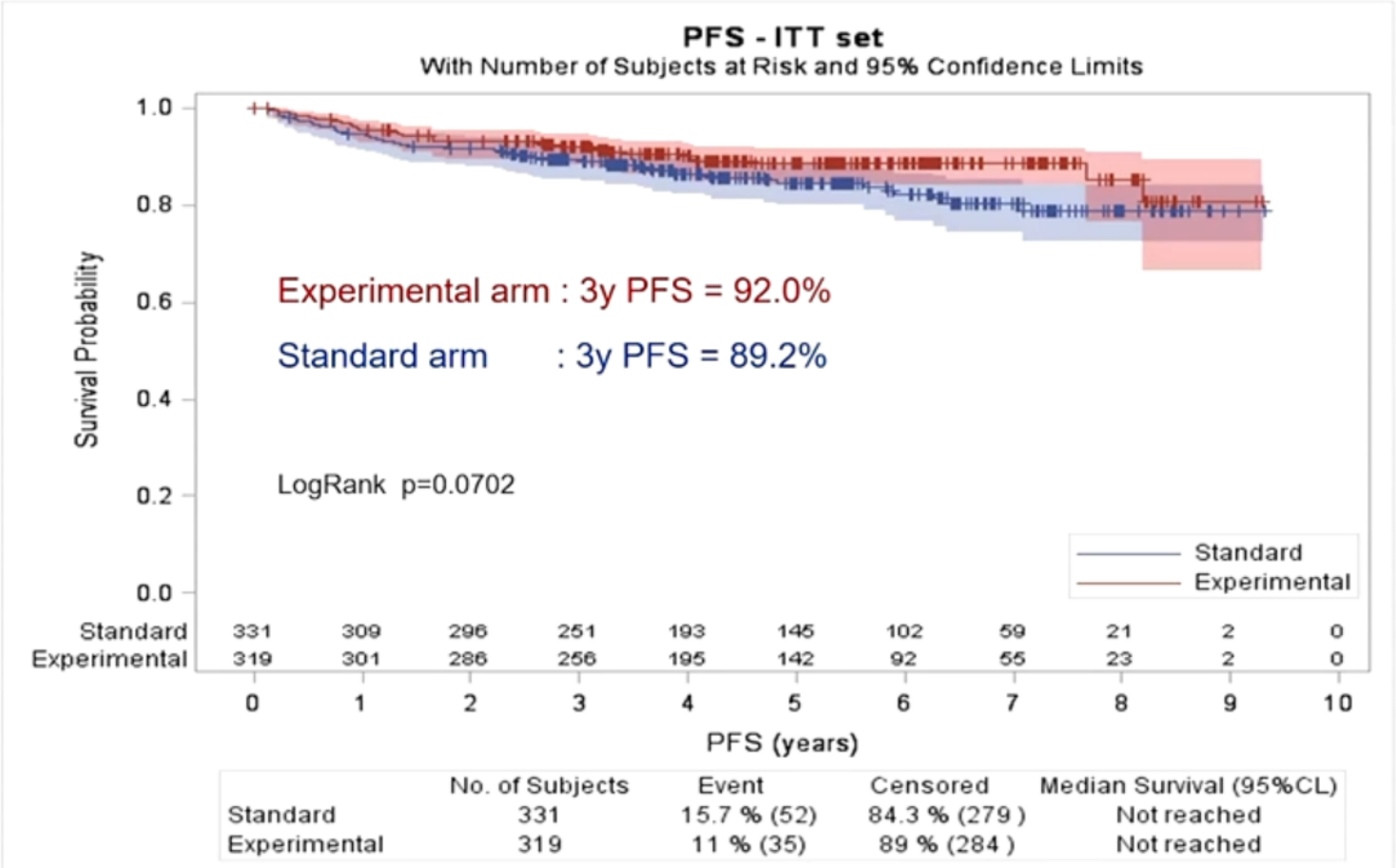
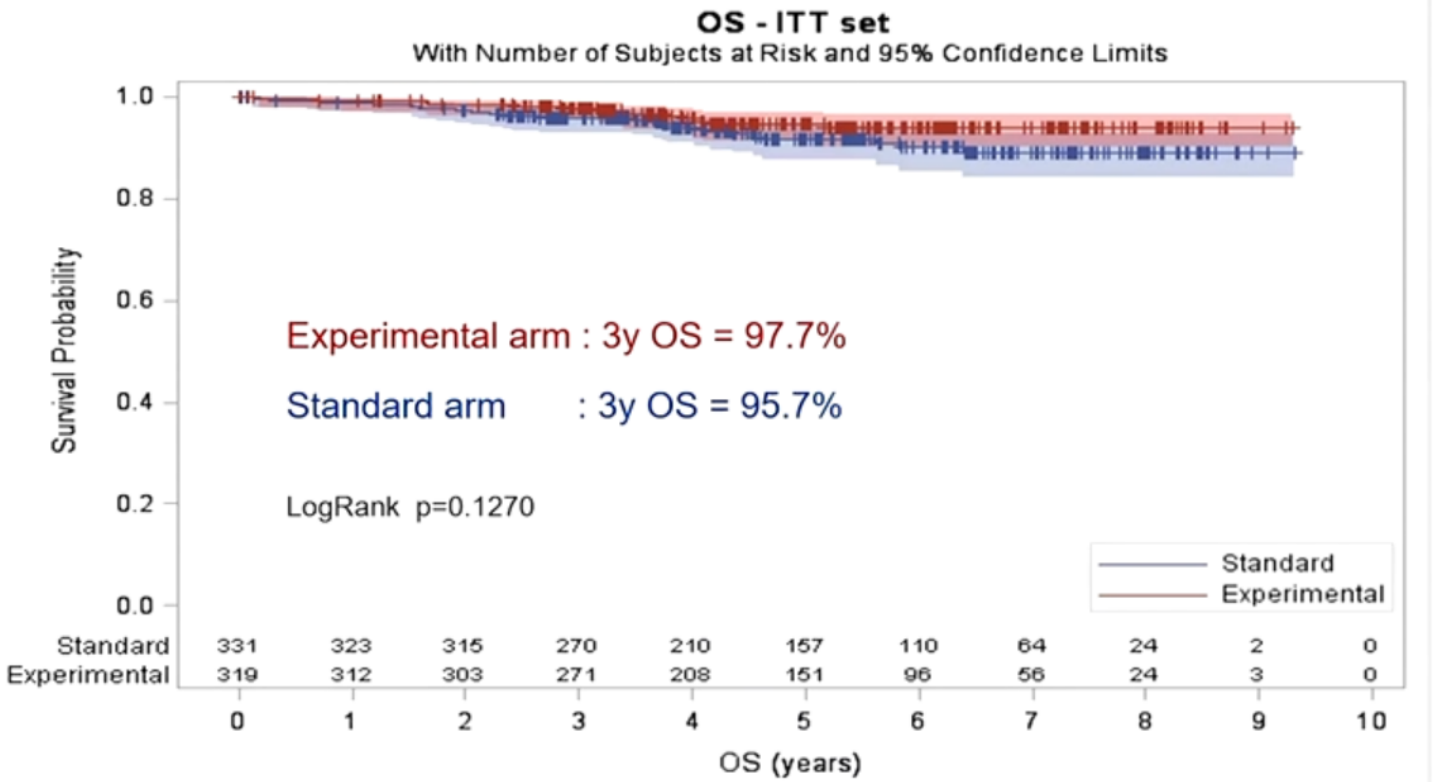
PFS – ITT set



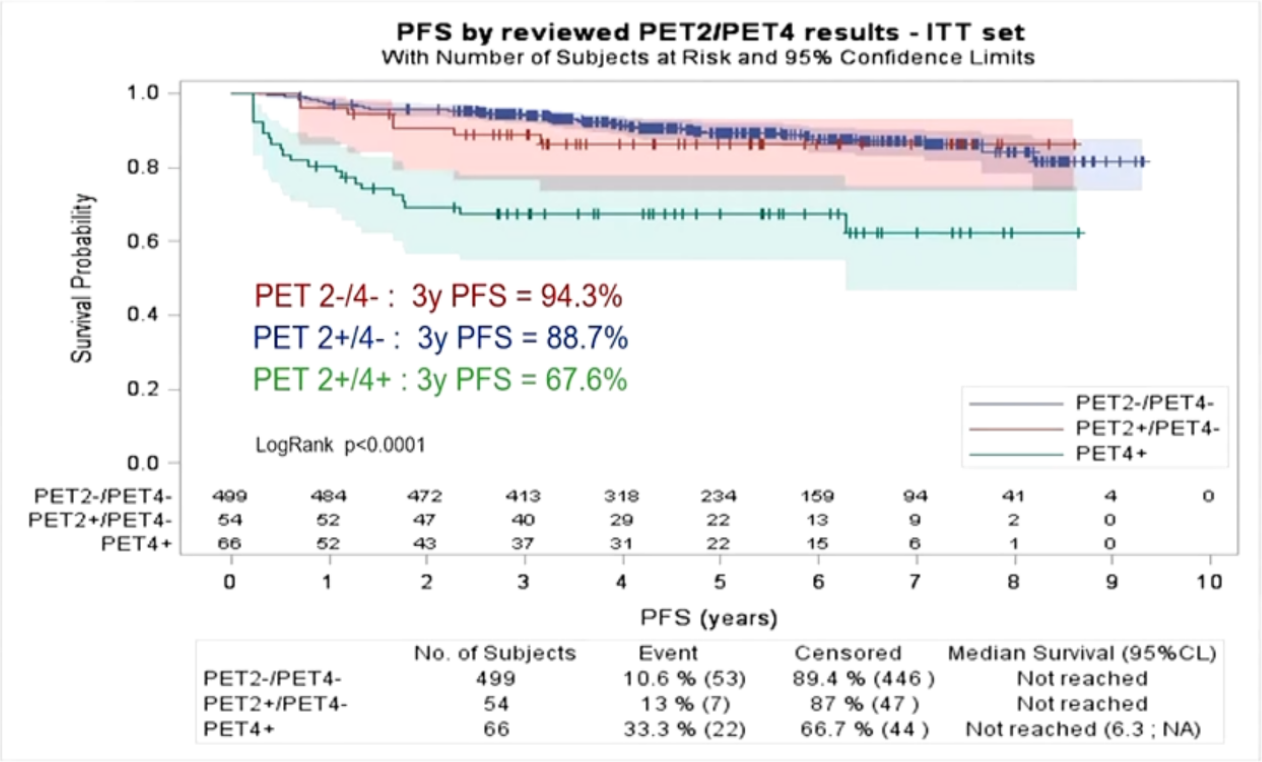
	No. of Subjects	Event	Censored	Median Survival (95%CL)
Standard	331	15.7 % (52)	84.3 % (279)	Not reached
Experimental	319	11 % (35)	89 % (284)	Not reached

OS – ITT set



	No. of Subjects	Event	Censored	Median Survival (95%CL)
Standard	331	7.9 % (26)	92.1 % (305)	Not reached
Experimental	319	4.7 % (15)	95.3 % (304)	Not reached

PFS by PET results in whole population



	No. of Subjects	Event	Censored	Median Survival (95%CL)
PET2-/PET4-	499	10.6 % (53)	89.4 % (446)	Not reached
PET2+/PET4-	54	13 % (7)	87 % (47)	Not reached
PET4+	66	33.3 % (22)	66.7 % (44)	Not reached (6.3 ; NA)

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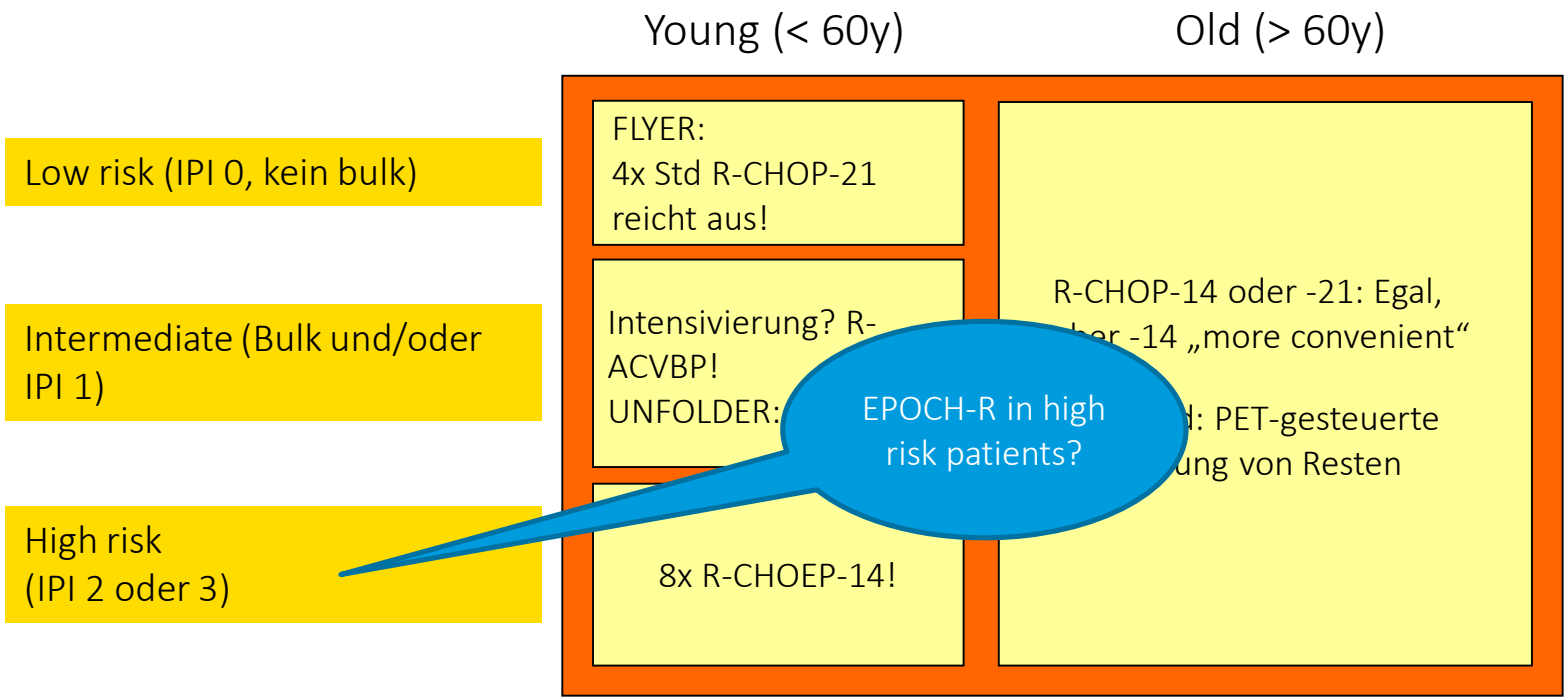
Erstlinien-Therapie des DLBCL: Zusammenfassung der DSHNHL Sicht



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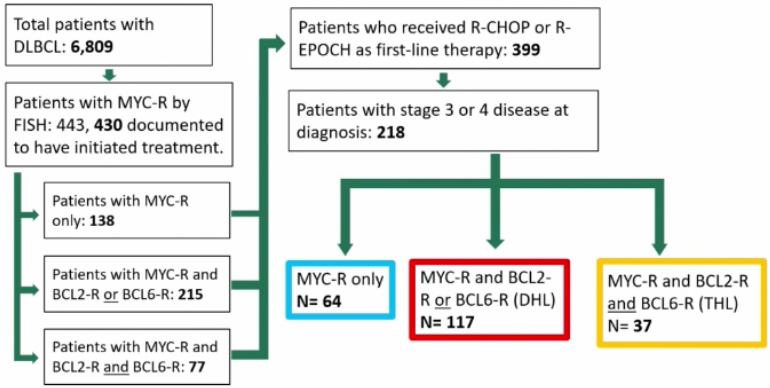
EHA S224: No difference in overall survival between R-CHOP and R-EPOCH among patient with advances stage MYC-rearranged, double hit, or triple hit diffuse large B-cell lymphoma.

Tylan Magnusson *et al.,* Birmingham AL, Vereinigte Staaten von Amerika

- Hintergrund:
- MYC-Rearrangements beim diffusen großzelligen B-Zell-Lymphom assoziiert mit schlechter Prognose
- Prognose verschlechtert sich bei gleichzeitigem Vorliegen eines Double-/Triple Hit-Lymphom (DHL/THL; sprich BCL2 und/oder BCL6 Rearrangements)
- Studien verweisen auf verbesserte Ergebnisse bei DHL/THL-Patienten bei Anwendung des R-EPOCH-Schemas, ohne jedoch ausreichende Evidenz für sichere Schlussfolgerungen zu haben
- Vergleich der Überlebensrate bei Patienten im fortgeschrittenem MYC-R DLBCL und DHL/THL behandelt mit R-CHOP und R-EPOCH: Sammlung und Analyse von Patientenakten der Datenbank Flatiron Health mit der Diagnose DLBCL (01.01.2011- 30.06.2020)

EHA S224: No difference in overall survival between R-CHOP and R-EPOCH among patient with advances stage MYC-rearranged, double hit, or triple hit diffuse large B-cell lymphoma.

Methods



Results: Patient characteristics

Characteristic		N (~%)	MYC-R	DHL	THL	R-CHOP	R-EPOCH
Total No. of patients		218	64	117	37	79	139
Sex	Female	94 (43)	24	54	16	36	58
	Male	124 (57)	40	63	21	43	81
Race	Asian	4 (2)	1	2	1	0	4
	Black	10 (5)	5	5	0	4	6
	Hispanic	11 (5)	3	5	3	4	7
	White	143 (66)	40	76	27	53	90
	Unknown	50 (23)	15	29	6	18	32
Age	≤ 60	65 (30)	23	30	12	19	46
	> 60	153 (70)	41	87	25	60	93
	Median	67.11	63.1	70.2	64.1	72.0	63.8
ECOG performance status	0/1	142 (65)	34	80	28	50	92
	≥ 2	15 (7)	7	7	1	6	9
	Missing	61 (28)	23	30	8	23	38
No. of extra nodal sites	0/1	155 (71)	41	89	24	54	100
	≥ 2	64 (29)	23	28	13	25	39
Lactate dehydrogenase	Normal	98 (45)	21	61	16	36	62
	Elevated	90 (41)	30	45	15	30	60
	Missing	30 (14)	13	11	6	13	17
First-line chemotherapy	R-CHOP	79 (36)	36	31	12		
	R-EPOCH	139 (64)	28 (44)	86 (74)	25 (68)		

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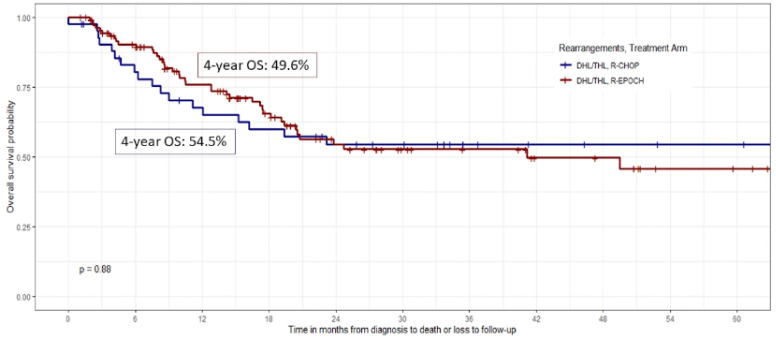
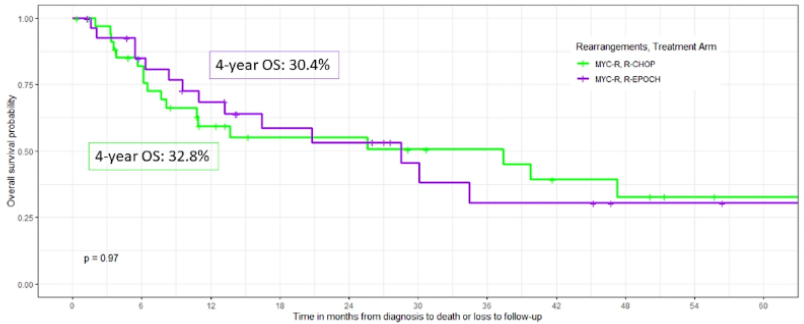
EHA S224: No difference in overall survival between R-CHOP and R-EPOCH among patient with advances stage MYC-rearranged, double hit, or triple hit diffuse large B-cell lymphoma.

Results: OS for advanced stage DHL/THL by treatment



Results: OS for advanced stage MYC-R alone by treatment



Signifikante Mortalitätsvariablen
(univariante Analyse des Behandlungstyps)

- LDH erhöht
- ECOG >/ = 2

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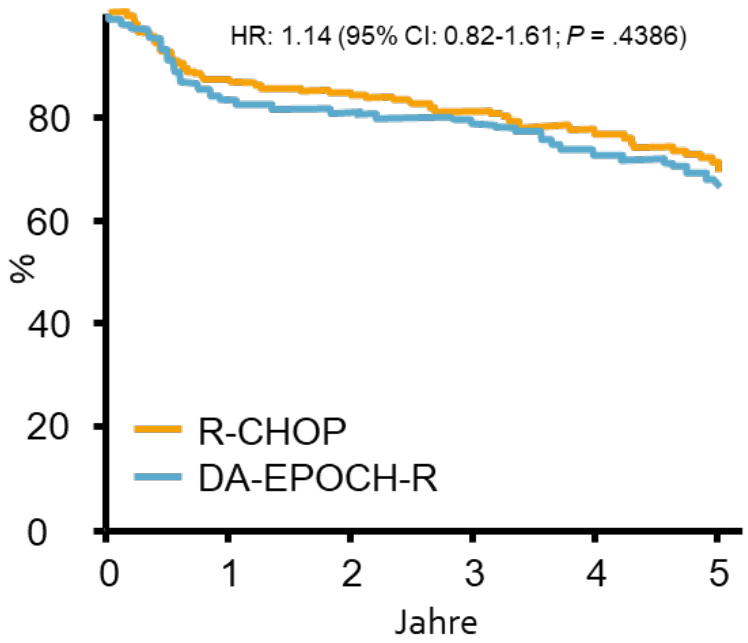
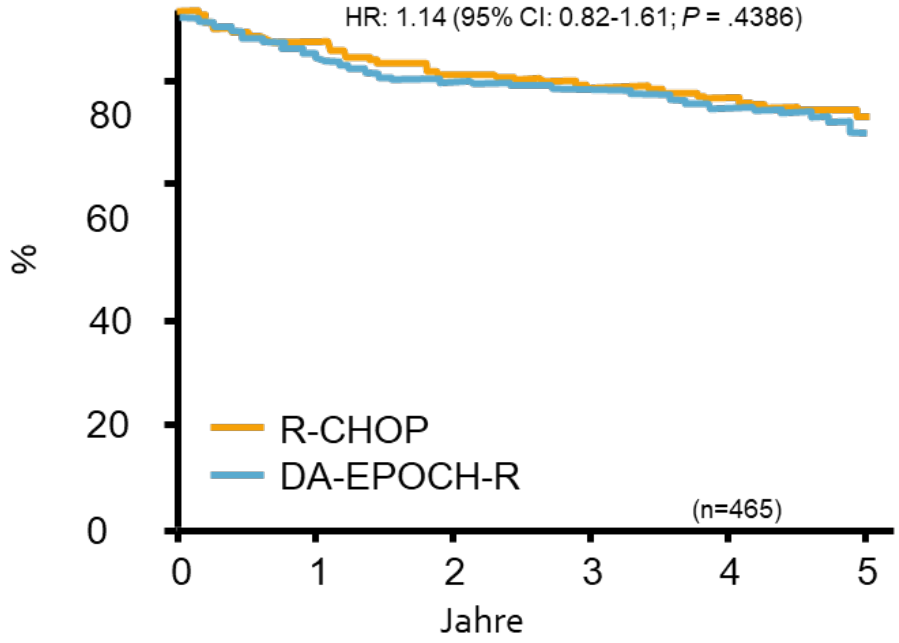
Das passt gut zu bekanntem Wissen: 6 x R-CHOP vs. 6 x DA-EPOCH-R

Ereignisfreies Überleben



Gesamtüberleben



Wilson et al., Blood 128(22): 469, 2016

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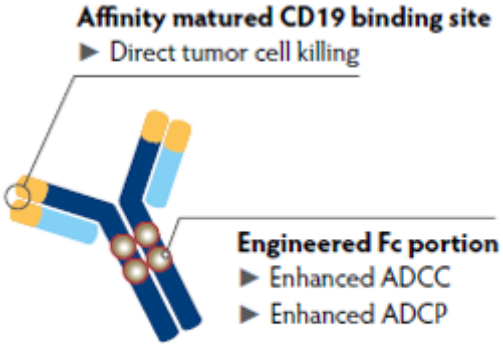

MOR208
tafasitamab

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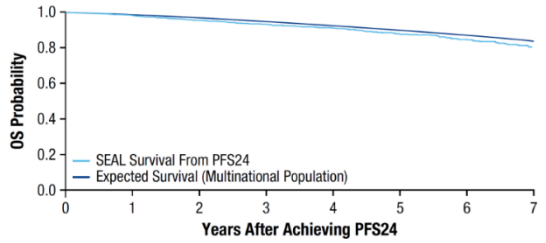
Outcome with R-CHOP based regimesn is either very good or very poor: Current salvage therapies are rather ineffective!

Figure 2. Overall Survival From Achieving PFS24 for Observed SEAL Patients and Expected Age- and Sex-Matched General Population

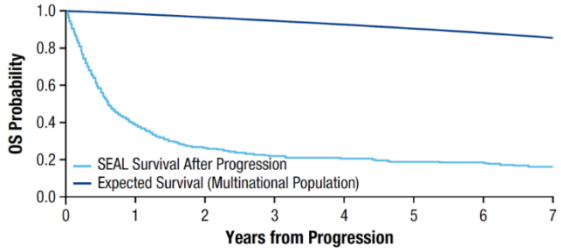


Achieved PFS24 n = 3678 (72%)		
OS after PFS24	**Observed**	**Expected**
3 years	93%	94%
5 years	88%	90%
7 years	80%	84%
SMR (95% CI)	1.22 (1.09-1.37)	

SEAL database = 14 global studies with rituximab as part of therapy

ANZINTER3 (n = 224), ECOG 4494 (n = 318), LNH031B (n = 110), LNH032B (n = 380), LNH036B (n = 602), MAIN (n = 787), DSHNHL 2002-1 MEGACHOEP (n = 262), MInT (n = 413), NHL13 (n = 741), PIX203 (n = 124), RICOVER-60 (n = 610), and RCHOP14v21 (n = 1080)

Figure 1. Overall Survival From Progression Within 24 Months (Fail to Achieve PFS24)



Failed to Achieve PFS24 n = 1423 (28%)

- Poor outcomes after progression
- Median OS = 7.2 months (95% CI, 6.8-8.1
- 5-year OS = 19%
- SMR = 32.1 (95% CI, 30.0-34.4)

OS, overall survival; PFS24, progression-free survival at 24 months; SMR, standardized mortality ratio.

Maurer, ASH 2016, #3072

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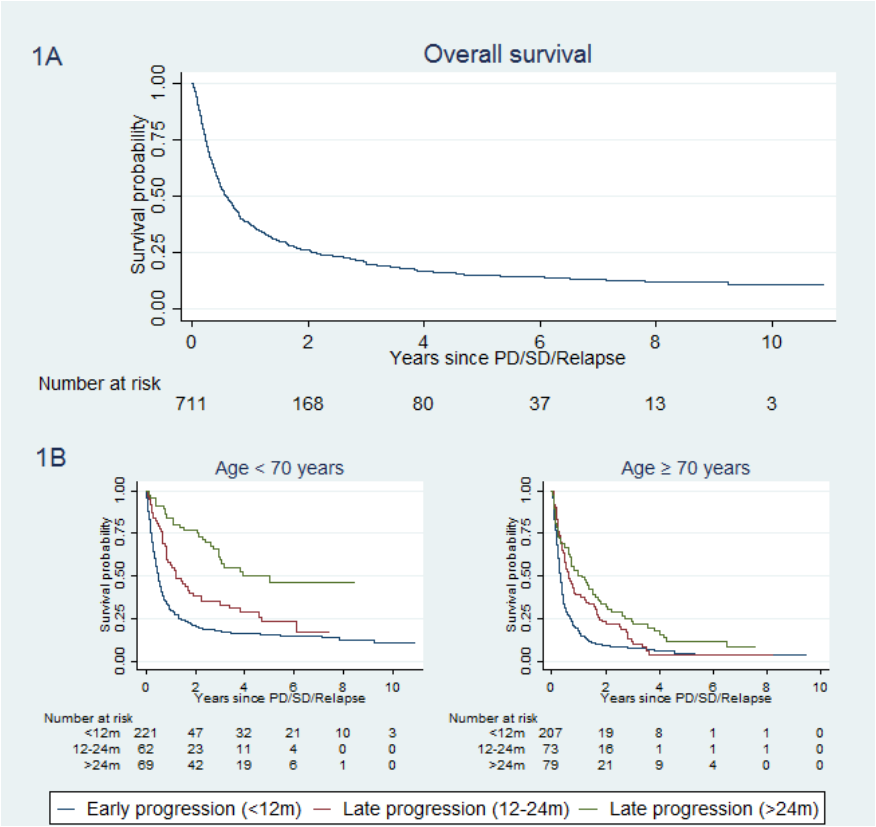
Prognosis of relapsed patients critically depends on time to relapse and age



- Most patients relapsed within 12 months (N=428, 60%)
- whereas 135 patients (19%) relapsed 12-24 months from diagnosis and
- 148 patients (21%) after 24 months.

< 70 y, 2-year OS was

- 21% for 0-<12,
- 38% for 12-24 and
- 77% for 24+

Karin Ekstrom Ekstroem Smedby et al., ASH 2019

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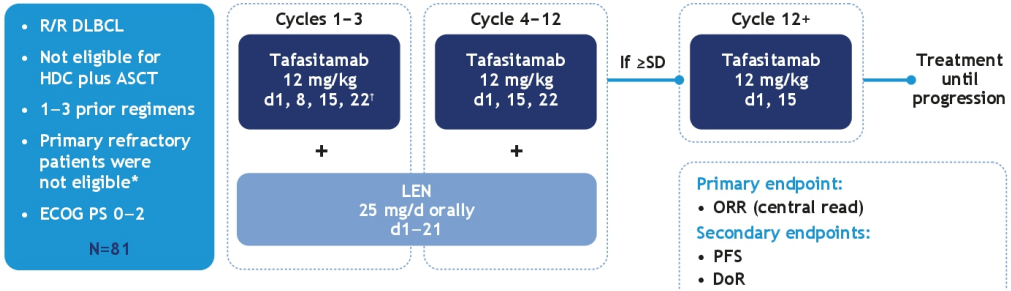
7513: Long-term analyses from L-MIND, a phase II study of tafasitamab (MOR208) combined with lenalidomide (LEN) in patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL). Johannes Düll *et al*., Würzburg, Deutschland (ASCO und ICML)

Fragestellung:

- Tafasitamab (= Fc-modifizierter, humanisierter, **anti-CD19 monoklonaler AK**) + Lenalidomide sind beim rezidivierten DLBCL wirksam (phase II study results published by Salles et al., Lancet Oncol., 2020 Jul;21(7):978-988)
- Patientenpopulation: non transplant-eligible patients.
- **ASCO:** ≥ 35 months follow-up (Cut-off: 30.10.2020): duration of remissions?



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7513: Long-term analyses from L-MIND, a phase II study of tafasitamab (MOR208) combined with lenalidomide (LEN) in patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL).

Tafasitamab plus LEN	1 prior treatment (N=40)	≥2 prior treatments (N=40)	Overall (N=80)
Best Objective Response, n (%)			
CR	19 (47.5)	13 (32.5)	32 (40.0)
PR	8 (20.0)	6 (15.0)	14 (17.5)
SD	7 (17.5)	6 (15.0)	13 (16.3)
PD	5 (12.5)	8 (20.0)	13 (16.3)
NE*	1 (2.5)	7 (17.5)	8 (10.0)
ORR (CR + PR), n (%) [95% CI]†	27 (67.5) [50.9–81.4]	19 (47.5) [31.5–63.9]	46 (57.5) [45.9–68.5]
Median DoR, months (95% CI)‡	43.9 (9.1–NR)	NR (15.0–NR)	43.9 (26.1–NR)
Median PFS, months (95% CI)‡	23.5 (7.4–NR)	7.6 (2.7–NR)	11.6 (6.3–45.7)
Median OS, months (95% CI)‡	45.7 (24.6–NR)	15.5 (8.6–NR)	33.5 (18.3–NR)

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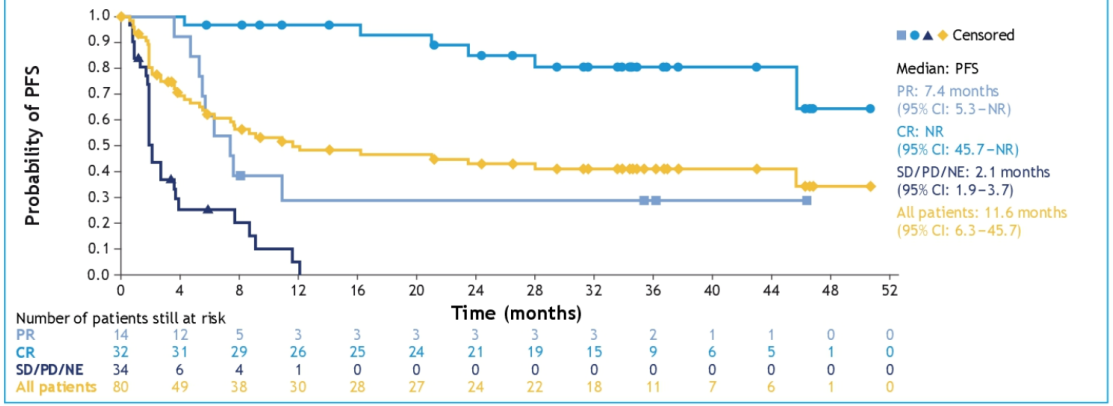
7513: Long-term analyses from L-MIND, a phase II study of tafasitamab (MOR208) combined with lenalidomide (LEN) in patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL).

Figure 3B. Progression-free survival by best response



CI, confidence interval; CR, complete response; NE, not evaluable; NR, not reached; PD, disease progression; PFS, progression-free survival; PR, partial response; SD, stable disease.

Median time since first DLBCL diagnosis, months (range) 26·9 (9–190), 50% 2nd line

- Gute Ergebnisse & gutes Sicherheitsprofil bei ASCT-ungeeigneten R/R DLBCL Patienten (günstige Patientenkohorte)
- anhaltende Remission und verbessertes Überleben, v.a. bei 1. Rezidiv
- Randomisierte Studie nötig
- ➢ Spannend wird in jedem Fall die Front-MIND Studie in der Erstlinientherapie (Start dieses Jahr)

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RE-MIND STUDY: COMPARISON OF TAFASITAMAB + LENALIDOMIDE (L-MIND) VS LENALIDOMIDE MONOTHERAPY (REAL-WORLD DATA) IN TRANSPLANT-INELIGIBLE PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA

Author(s): Pier Luigi Zinzani, Thomas Rodgers, Dario Marino, Maurizio Frezzato, Anna Maria Barbui, Claudia Castellino, Erika Meli , Annarita Conconi, Nicola Cascavilla, Federica Cavallo, Nathan H. Fowler, Bruce Feinberg, Sascha Tillmanns, Stephan Parche, Günter Fingerle-Rowson, Mark Winderlich, Sumeet Ambarkhane , Gilles Salles, Grzegorz Nowakowski

EHA Library. Zinzani P. 06/12/20; 295058; S238

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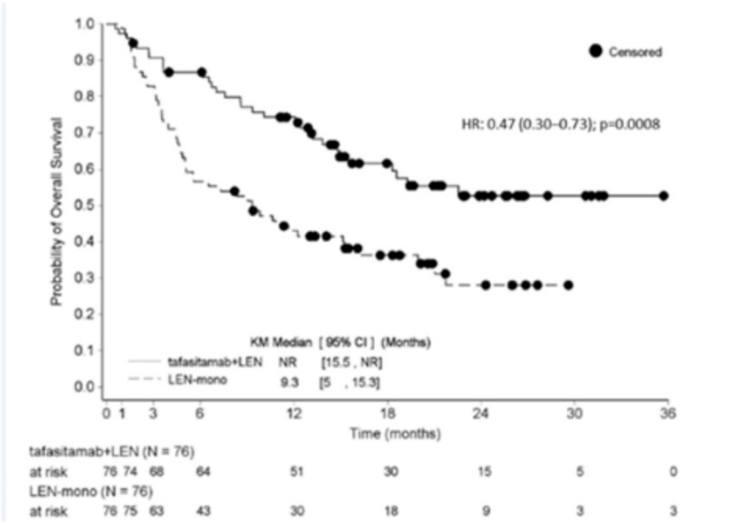
Is L-MIND combination better than lenalidomide? Real-world comparison

Design

- 490 patients from 58 centers were included
- Patients were treated with initial dose of lenalidomide of 25 mg/day
- Nearest neighbor 1:1 matching methodology; balanced for nine parameters

Figure 1. Overall survival



CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; Mono, monotherapy; NR, not reached.

Zinzani et al. EHA, #S238

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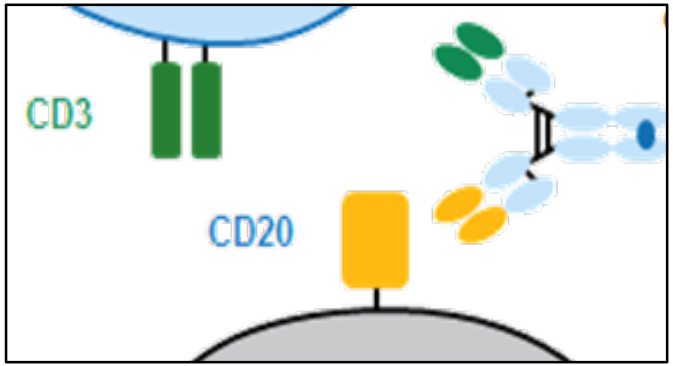

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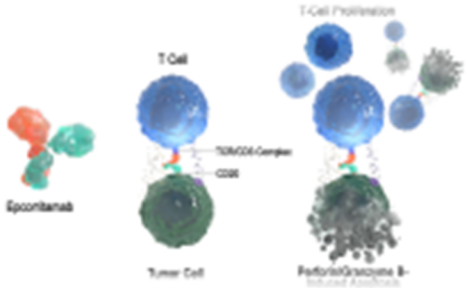
EHA EP499: SUBCUTANEOUS EPCORITAMAB IN PATIENTS WITH RELAPSED/REFRACTORY B-CELL NON-HODGKIN LYMPHOMA: SAFETY PROFILE AND ANTI-TUMOR ACTIVITY

Rogier Mous *et al.,* Utrecht, Niederlande

- Hintergrund:
- Epcoritamab: CD20xCD3 spezifischer Antikörper
- Induziert T-Zell-vermittelten Zelltod von CD20-positiven B-Zellen
- Präsentation aktueller Daten der ersten Phase1/2-Studie mit Epcoritamab bei Patienten mit rezidiviertem oder refraktärem (r/r) B-Zell-Non-Hodgkin-Lymphom (B-NHL; NCT03625037).



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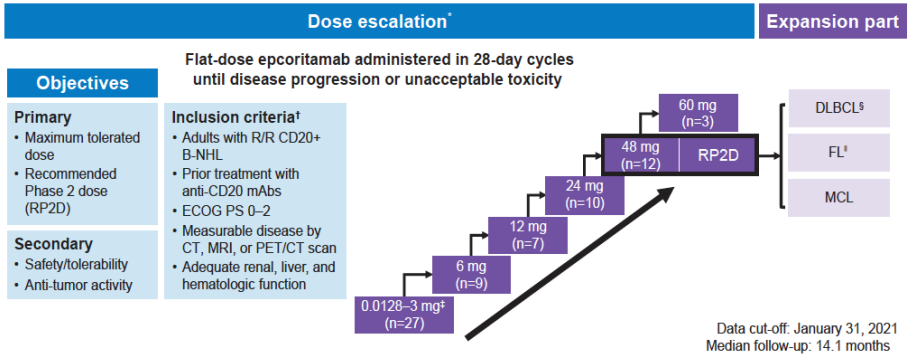
Phase I/II - Step-up-Dosing zur Prophylaxe eines Zytokinfreisetzungssyndroms

Figure 2. EPCORE NHL-1 Study Design



AEs by Preferred Term, n (%)	AE Severity		
	Grade 1–2	Grade 3	Grade 4
Pyrexia*	43 (63)	4 (6)	0
Cytokine release syndrome	40 (59)	0	0
Injection site reaction	32 (47)	0	0
Fatigue	26 (38)	4 (6)	0
Diarrhea	18 (26)	0	0
Hypotension*	17 (25)	4 (6)	0
Dyspnea	16 (24)	0	1 (1)
Tachycardia*	14 (21)	0	0
Anemia	7 (10)	9 (13)	0

*Most pyrexia, hypotension, and tachycardia events were symptoms of cytokine release syndrome.

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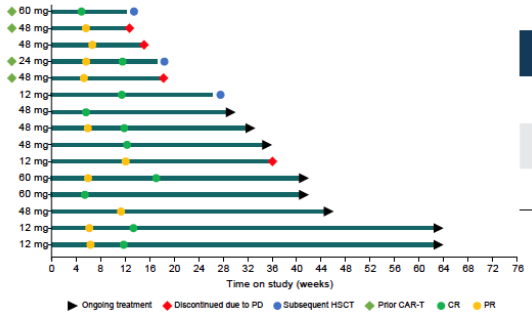
Cut Off: 31.1.2021 n=68 mit B-NHL

	DLBCL
Anzahl	46 67,6%
Vorbehandlung	3 (1-6)
Follow-Up	10,2
Overall Response Rate	≥12mg (n=22): 68% (CR=46%; PR=23%) ≥48mg (n=11) 91% (CR=55%; PR=36%)
PR zu CR im Verlauf	6
Zeit bis zum Ansprechen	1,4 Monate (1-4)
Zeit bis CR	2,7 (1,1-3,9)
PFS	≥12 mg (n=22): 9,1 Monate ≥48mg: not reached

Figure 4B. Response profile in patients with R/R DLBCL



Response Parameter	≥12 mg (n=22)	48–60 mg (n=11)
Median follow-up, months	9.3	8.8
Median TTR, months (range)	1.4 (1–4)	1.3 (1–3)
Median DOR, months (range)	NR (1.41+, 12.45+)	NR (1.41+, 12.45+)

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   - CD19 targeting CAR T-cell therapies

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EHA S216: First results of DLBCL patients treated with CAR-T cells and enrolled in DESCAR-T registry, a French real-life database for CAR-T cells in hematologic malignancies.

Steven Le Gouill *et al.,* Nantes, Frankreich

Hintergrund:

- ALL & BLBCL Patienten, behandelt mit der CAR-T Zell-Therapie, wurden in dem französischen DESCAR-T Register aufgenommen
- Sammlung realer Daten vom Behandlungsbeginn bis 15 Jahre danach
- Seit 2019 zugelassen und Referenzregister für Therapie-Rückerstattung der französischen Gesundheitsbehörden
- Verbunden mit komplementären Registern (wie Immunmonitoring-Datenbank, Bildplattform & Tumor-Biobank)

➢ Darstellung der ersten Analyse des Outcomes und Charakteristiken von DLBCL-Patienten der Datenbank

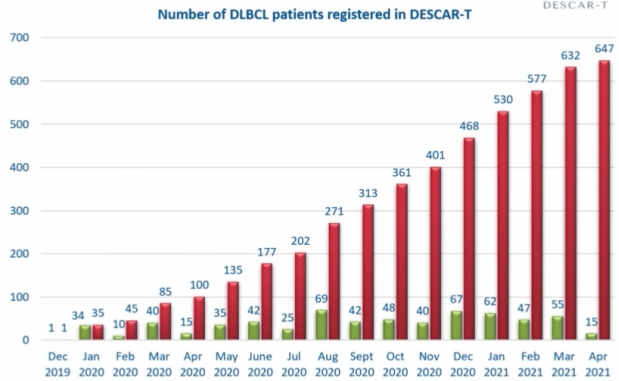
RESULTS: INCLUSIONS

Date: 12/04/2021

23 sites are qualified for CAR-T cells therapy and DESCAR-T

19 enrolling sites

Number of enrolled patients :
N = 647 DLBCL



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EHA S216: First results of DLBCL patients treated with CAR-T cells and enrolled in DESCAR-T registry, a French real-life database for CAR-T cells in hematologic malignancies.

PATIENTS' CHARACTERISTICS

	CAR-T ORDERED TREATED PTS (N=550)	CAR-T ORDERED UNTREATED PTS (N=53)
SEX (M / F)	331 / 219	36 / 17
MEDIAN AGE AT CAR-T ORDER (range)	63 (18-79)	65 (39-76)
>= 65yrs	229 (44%)	26 (51%)
DIAGNOSIS AT REGISTRATION		
DLBCL, NOS	482 (90%)	46 (90%)
PMBL	21 (4%)	0
HGBL, with MYC, BCL2 and/or BCL6 rearrangements	9 (1.7%)	4 (7.8%)
Other(s) / Missing	23 / 15	1 / 2
aaIPI AT REGISTRATION		
0-1	226 (45.7%)	11 (23%)
2	239 (48.3%)	28 (58.3%)
3	30 (6.1%)	9 (18.8%)
Missing	55	5
MEDIAN LINE OF TREATMENT (Range)	3 (1;10)	3 (2;7)
Auto-SCT / Allo-SCT	121 (22.5%) / 10 (2%)	5 (9.6%) / 1 (2%)
RESPONSE AFTER BRIDGING (n=441; 80.2%)		
CR	37 (8.4%)	/
PR	83 (18.8%)	/
SD	53 (12%)	/
PD	239 (54%)	/
Not Evaluated / Missing	16 (3.6%) / 13 (2,9%)	/
MEDIAN TIME FROM CAR-T ORDER TO TTT (days; Q1-Q3)	50 (43;60)	/

Early CRS, neurotox, and infections

	Patients with at least one CAR-T specific toxicity within 10 days N=280
ICU hospitalization	102 (36.4%)
Treated for CAR-T specific tox	230 (82.1%)
Tocilizumab	194 (69.3%)
Siltuximab	12 (4.3%)
Corticosteroïds	135 (48.2%)

Axi-cel

	Patients with at least one CAR-T specific toxicity within 10 days N=147
ICU hospitalization	37 (25.2%)
Treated for CAR-T specific tox	95 (64.6%)
Tocilizumab	84 (57.2%)
Siltuximab	1 (0.7%)
Corticosteroïds	41 (27.9%)

Tisa-cel

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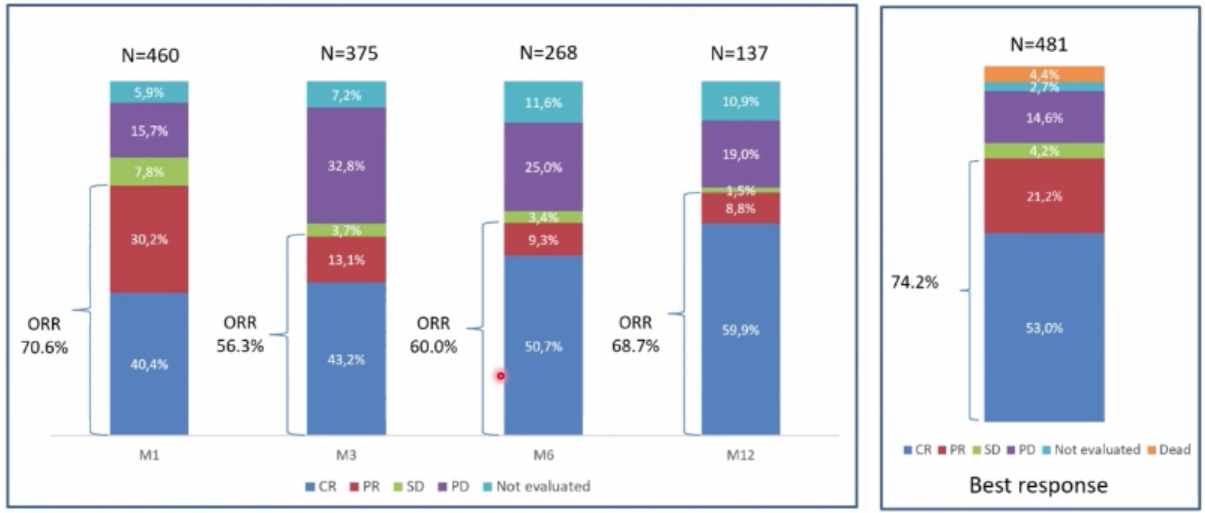

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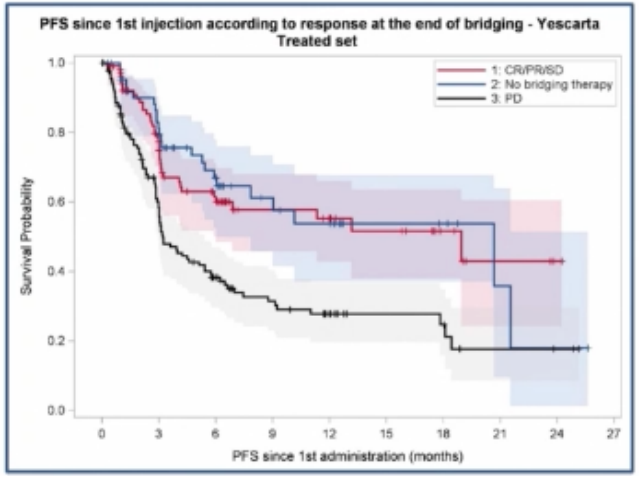
Axi-cel

PFS at 6 months[#]:

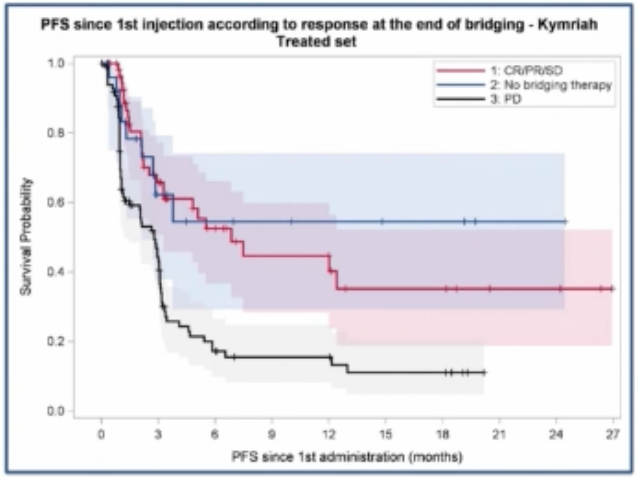
- CR/PR/SD = 61.4% [50– 71] (n=116)
- No bridging = 66.9% [52.5 – 77.9] (n=75)
- PD = 38.2% [29.5 – 46.9] (n=139)



Tisa-cel

PFS at 6 months * :

- CR/PR/SD = 52.5% [36.7 – 66] (n=57)
- No Bridging = 54.4% [29.2 – 74.1] (n=34)
- PD = 17.1% [9.7 – 26.4] (n=100)



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EHA S255: Polatuzumab Vedotin vs. CAR- T cell for patients with relapsed/refractory diffuse large B-cell lymphoma – a propensity score matched analysis.

Irit Avivi *et al.,* Tel Aviv, Israel

Hintergrund:

- Verglichen mit konventioneller Chemotherapie bei Patienten mit rezidivierenden/refraktären DLBCL besseres Ergebnis durch CAR-T Zellen-Therapie & Polatuzumab-Bendamustin-Rituximab Therapie
- Umstritten bleibt die Reihenfolge der Therapiemöglichkeiten

R/ R- DLBCL- Behandlung der Patienten mit CAR-T oder Pola/Pola BR im Zeitraum vom 01/2019 - 08/2020 nach >/ = 2 versagten Behandlungslinien

Propensity-Score-Analyse:
Abgleich basierend auf Alter, transformed/de novo, COO, Anzahl vorheriger Therapielinien, ECOG-PS, LDH

Analyse:
Ansprechrate, progressionsfreies Überleben (PFS), Gesamtüberleben (OS)

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EHA S255: Polatuzumab Vedodtin vs. CAR- T cell for patients with relapsed/refractory diffuse large B-cell lymphoma – a propensity score matched analysis.

Domain	P value	Pola group (n= 49)	CAR- T Group (n= 49) *
Age	.38	67 (23- 92)	70 (20- 85)
Sex, female	.68	21	23
Transformed vs De Novo DLBCL	.48	16	14
Non-GCB	.53	27	30
No prior lines	.43	3 (2- 7)	2 (2- 8)
ECOG PS > 1	.1	23	31
Elevated LDH	.8	38	39

*
Axicabtagene ciloleucel, N=14;
Tisagenlecleucel, N=35

Patient Characteristics (II)

Pola treated patients (n=41)
Pola-BR, n=31 ; Pola-R, n=10
Average bendamustine dose per cycle -75.5 mg/m2 (35-90)
Median number of cycles - 4 for Pola-BR and 5 for Pola-R

CAR-T treated patients (n=41)
Bridging therapy – 30(73%)
steroids (n=1, 2.4%), Radiation (n=4, 9.8%), Chemotherapy (n=25, 61%).

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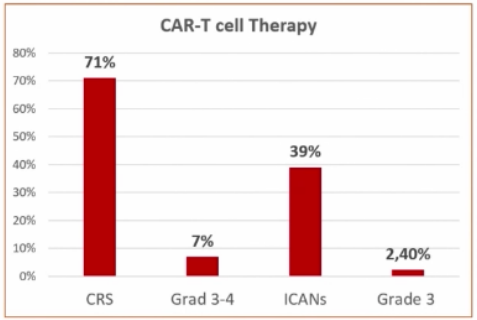
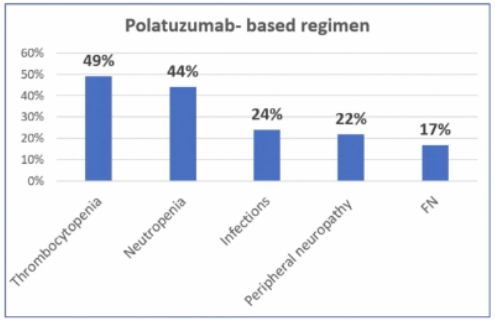
Adverse Events



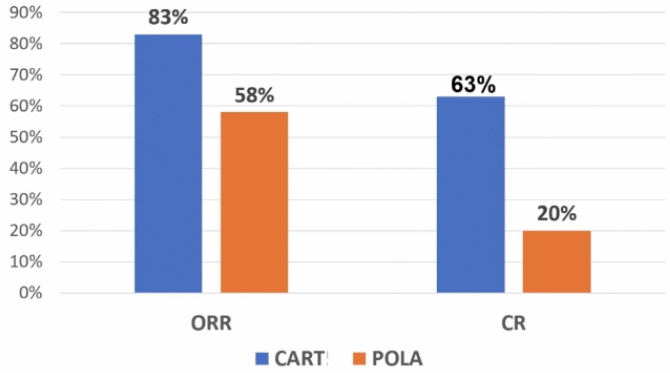
TRM: 0%



TRM: 7.3% (n=3)

Late Toxicities: Late cytopenia- 22% (n=9), all eventually recovered.
Hypogammaglobinemia ,14 (34%) ,not associated with subsequent infections.

Response Rate



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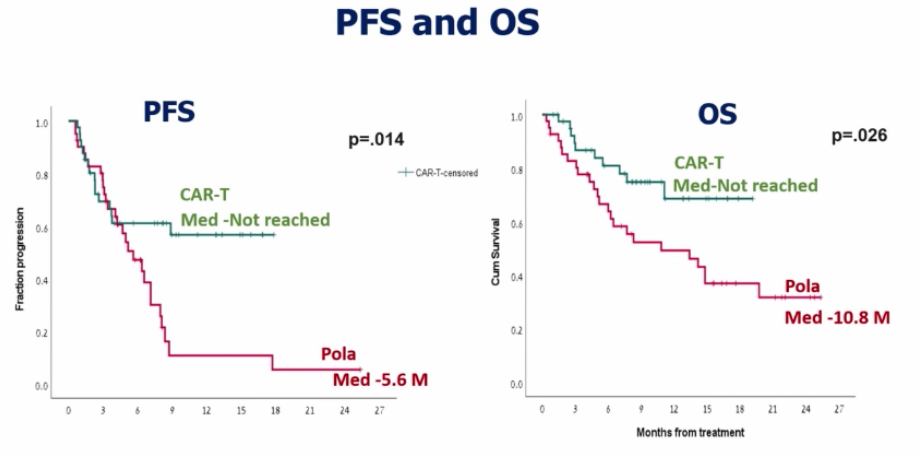

- CAR-T gegenüber Pola-BR) bei R/R- DLBCL Patienten: Tendenz zu verlängertem PFS (not reached vs 5.6 months) und OS (not reached vs 10.8 months), besonders ausgeprägt bei Patienten mit erhöhter LDH
- Pola-BR sind gut vergleichbar mit den publizierte Zulassungsdaten, obwohl in dieser Analyse die Patienten mit geringeren B Dosen behandelt wurden
- Die Autoren schlussfolgern, dass trotz der Limitationen retrospektiver Analysen die gefundenen Unterschiede relevant sind und CAR T-Zelltherapie in dieser Situation für die Patienten einen wesentlichen Vorteil hinsichtlich der Wirksamkeit bieten

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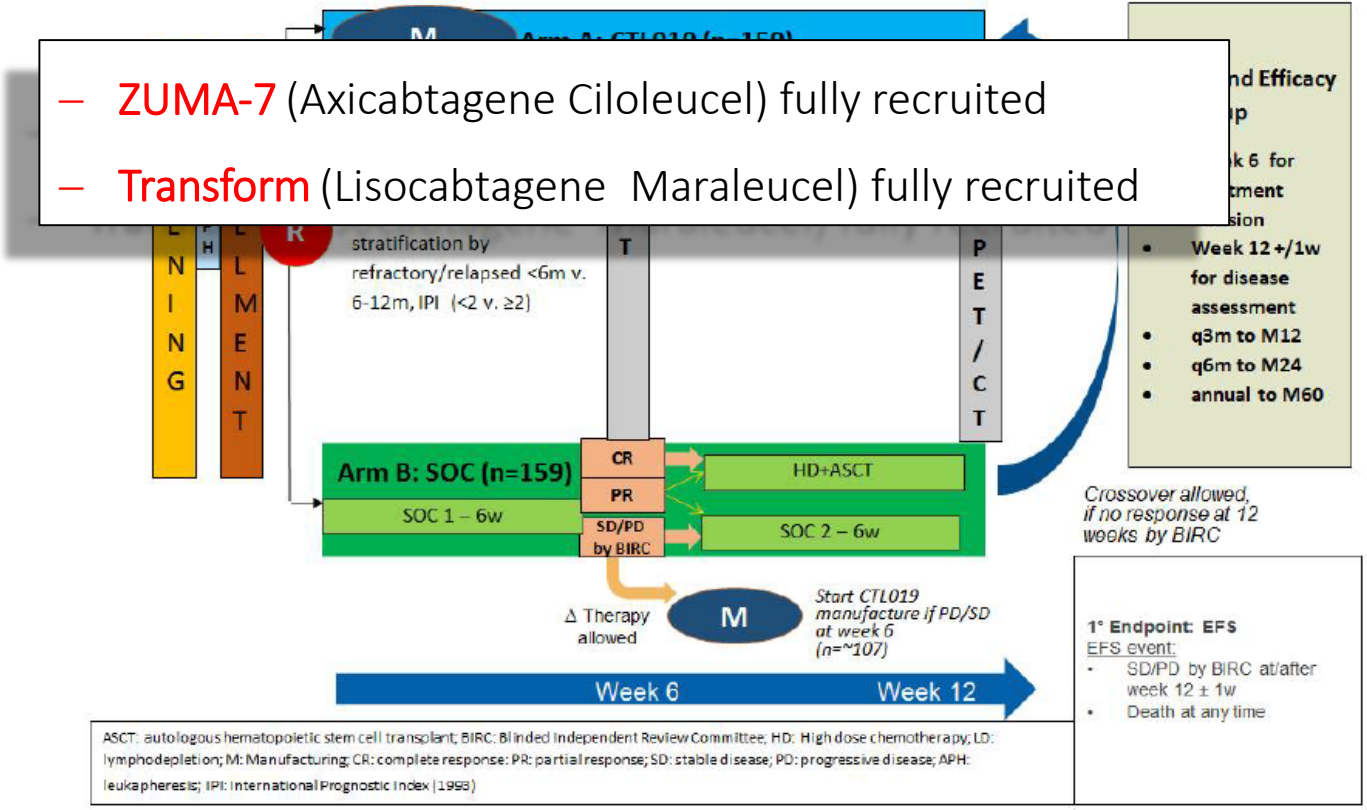
Perspectives: CD19 CARs better than HDCT in 2nd line ? Phase III studies.

BELINDA:
Tisagenlecleucel versus standard of care in adult patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma:
A randomized, open label, phase III trial

- ZUMA-7 (Axicabtagene Ciloleucel) fully recruited
- Transform (Lisocabtagene Maraleucel) fully recruited



Breaking News – Interim analysis of the phase 3 TRANSFORM trial reports significant clinical benefit of Liso-cel treatment over SOC in transplant-eligible 2L r/r LBCL

BMS press release, June 10th 2021

Bristol Myers Squibb Announces Positive Topline Results from Phase 3 TRANSFORM Trial Evaluating Breyanzi (lisocabtagene maraleucel) Versus Chemotherapy Followed by Stem Cell Transplant in Second-line Relapsed or Refractory Large B-cell Lymphoma

06/10/2021

CATEGORY: Corporate/Financial News

Study met primary and key secondary endpoints, demonstrating a highly statistically significant improvement in event-free survival, complete response rate and progression-free survival compared to standard of care

Breyanzi safety results consistent with data from pivotal TRANSCEND NHL 001 trial

Results represent the first time a therapy has demonstrated benefit compared to high-dose chemotherapy and stem cell transplant in relapsed or refractory large B-cell lymphoma, and support the potential of Breyanzi in earlier lines of therapy in this patient population

- Liso-cel is the first CAR T to demonstrate **superior efficacy over SOC in 2L transplant-eligible r/r LBCL**
- Data will be presented at an upcoming medical conference

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DLBCL: status quo 2021

1. First line

2. Later lines: revival of Immunotherapy
   - Naked CD19 antibody plus lenalidomide
   - „antibody drug conjugates“
   - CD3xCD20 bispecific antibodies
   - CD19 targeting CAR T-cell therapies

3. Summary and perspectives

DLBCL: status quo 2021

1. First line

2. Later lines: revival of Immunotherapy
   - Naked CD19 antibody plus lenalidomide
   - „antibody drug conjugates“
   - CD3xCD20 bispecific antibodies
   - CD19 targeting CAR T-cell therapies

3. Summary and perspectives

1. **PET-guided 4x R-CHOP aaIPI 0?**

2. Later lines: revival of Immunotherapy
   - Tafasitamab FDA zugelassen, verfügbar, 1st line Studie startet 2021
   - „antibody drug conjugates“
   - Entwicklung rasant und interessant!
   - Verlässliche Registerdaten aus Frankreich bestätigen Ergebnisse aus den Zulassungsstudien