Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

13.– 16. Juni 2019

KML-Experten berichten vom EHA 2019 in Amsterdam

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT EHA Amsterdam 13.– 16. Juni 2019

Prof. Dr. med. Peter Borchmann

CAR-T-Zell-Therapien

Klinik I für Innere Medizin der Uniklinik Köln|
Co-Chairman der Deutschen Hodgkin Studiengruppe (GHSG)

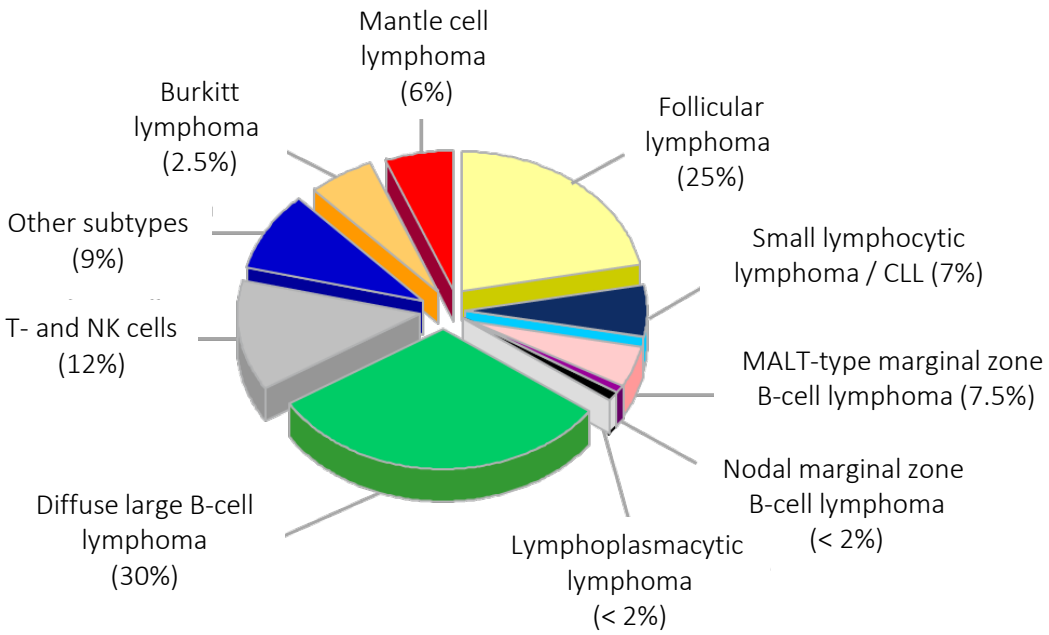
Disclosures: P. Borchmann

- Advisory role or expert testimony: Amgen, Bristol-Myers Squibb, Celgene Corporation, Miltenyi Biotech, Novartis, Roche, Takeda Oncology
- Honoraria: Bristol-Myers Squibb, Celgene Corporation, Miltenyi Biotech, MSD, Novartis, Roche, Takeda Oncology
- Scientific research funding: Amgen, Novartis, Takeda Oncology

Kapitel 1

Welche Patienten werden mit CAR-T-Zellen behandelt?

In focus: diffuse large B-cell non-Hodgkin lymphoma



1st-line combined immuno-chemotherapy (R-CHO(E)P) is highly effective:

OS at 3 years around 75%

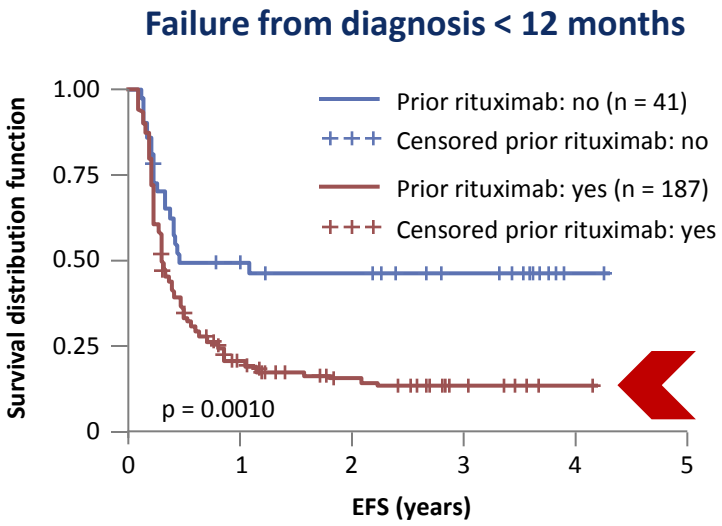
Median age at 1st diagnosis 70 years, 75% of all patients > 60 years of age

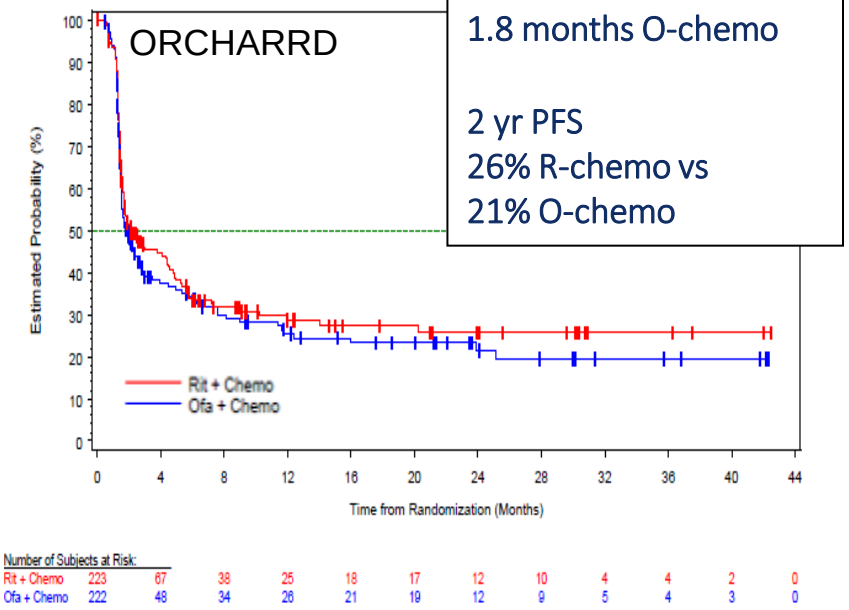
CLL, chronic lymphocytic leukaemia; MALT, mucosa-associated lymphoid tissue; NK, natural killer; OS, overall survival; R-CHO(E)P, rituximab, cyclophosphamide, doxorubicin, vincristine, (etoposide), and prednisone.

Lichtman MA. Williams Hematology. (7th Ed). New York, NY: McGraw Hill, 2006;1408. Pfreundschuh M, et al. Lancet Oncol. 2008;9:105-16. Pfreundschuh M, et al. Lancet Oncol. 2011;12:1013-22. Schmitz N, et al. Lancet Oncol. 2012;13:1250-9.

Developments for younger patients with DLBCL in the last decade

3 cycles of salvage-Tx, followed by HDCT plus APBSCT is standard of care





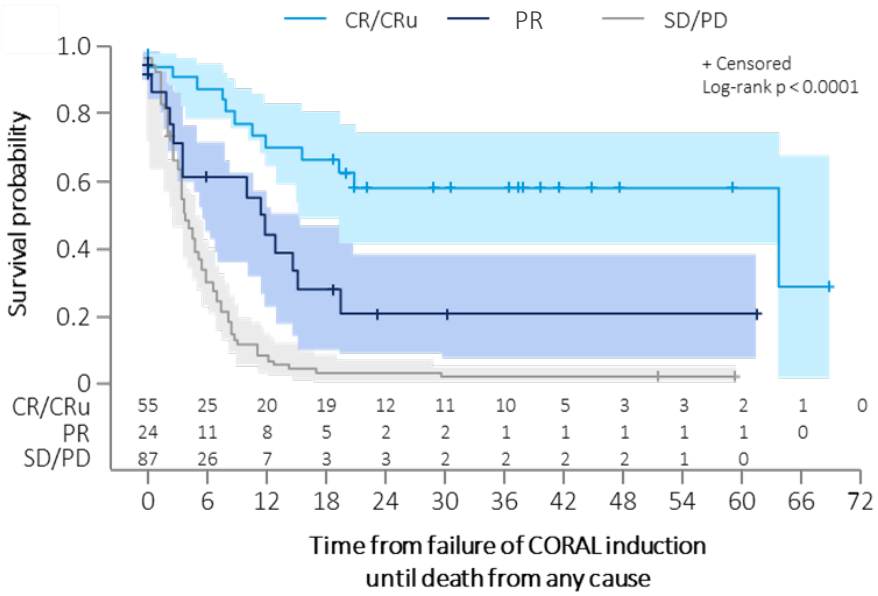
Median PFS
2.1 months R-chemo vs
1.8 months O-chemo

2 yr PFS
26% R-chemo vs
21% O-chemo

HDCT, high-dose chemotherapy; O-chemo, ofatumumab chemotherapy; R-chemo, rituximab chemotherapy; Tx, treatment.

Gisselbrecht C, et al. J Clin Onol. 2010;28:4184-90.
van Imhoff GW, et al. Blood 2014;124:630. Presented at ASH 2014.

PFS according to response status and number of patients proceeding to transplantation



	Enrolled	Transplanted
CORAL	400	206
ORCHARD	447	157
NCIC-CTG LY.12	619	307

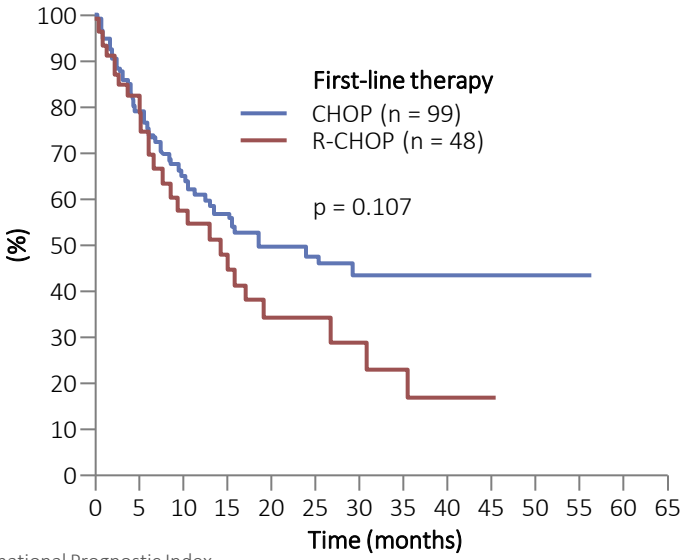
Transplanted patients: 35–50%

CR/Cru, complete response/ complete response unconfirmed;
PD, progressive disease; PR, partial response; SD, stable disease.

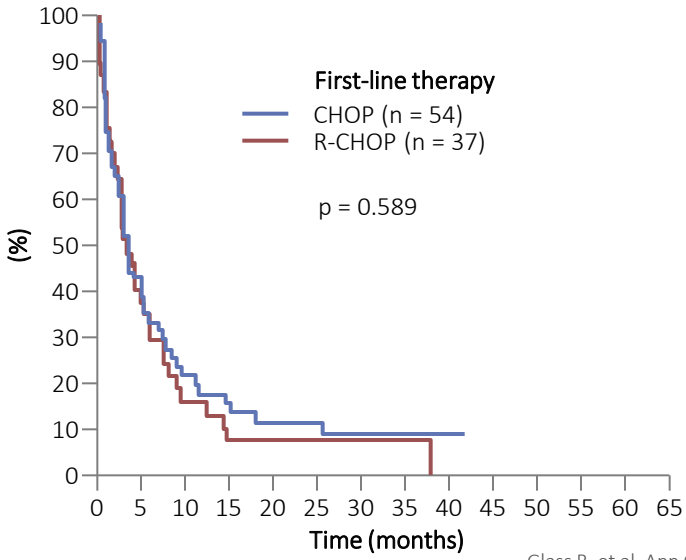
van Den Neste E, et al. Bone Marrow Transplant. 2016;51:51-7.
van Imhoff GW, et al. J Clin Oncol. 2017;35:544-51.

Lymphoma progression in older patients
RICOVER-60 trial: survival after progression

Relapse after remission



Progressive disease



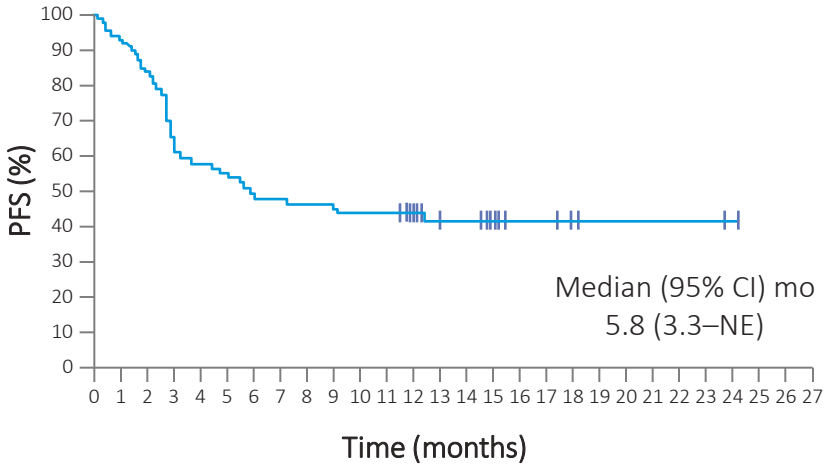
IPI, International Prognostic Index.

Glass B, et al. Ann Oncol, 2017;28:3058-64.

- Risk factor ”time to progression”: < / > 12 months
- Median OS < 6 months in patients relapsing within 12 months from 1st line
- High-dose chemotherapy with autologous stem cell support without any impact on OS (after adjusting for IPI)

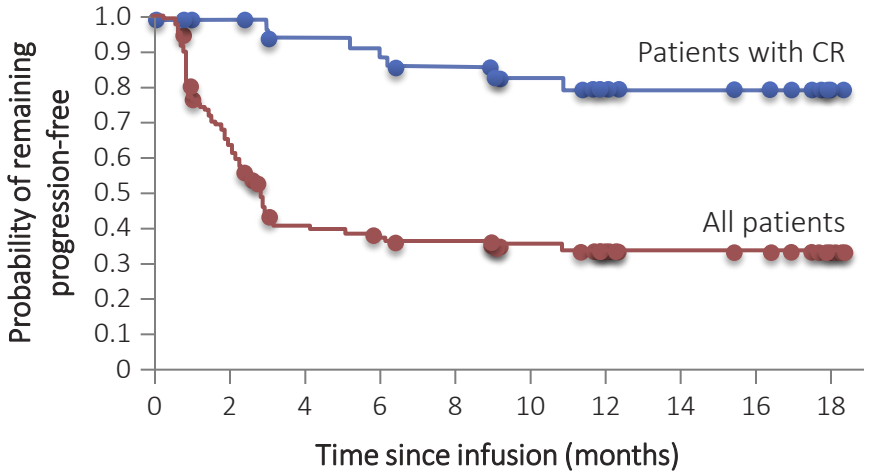
Summary of approved products after two prior regimens: PFS

Axicabtagene ciloleucel
Yescarta
ZUMA-1 phase 2 trial



Number at risk	108	101	90	71	61	58	52	50	49	49	47	47	34	21	20	12	6	6	4	3	3	3	3	3	1	0

Tisagenlecleucel
Kymriah
JULIET phase 2 trial



Number at risk																										
Patients with CR	40	39	39	36	35	35	33	31	31	29	24	23	15	9	9	9	8	7	2							
All patients	111		65		38		34		32		25		16		10		9		3							

Neelapu SS, et al. N Engl J Med. 2017;377:2531-44.
Schuster SJ, et al. N Engl J Med. 2019;380:45-56.

Kapitel 2

Real-World-Data: Erste Anwendungsdaten aus Europa nach der Zulassung

CAR T in DLBCL: real world experience

S1600

REAL-WORLD RESULTS ON CD19 CAR T-CELL FOR 60 FRENCH PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA INCLUDED IN A TEMPORARY AUTHORIZATION FOR USE (ATU) PROGRAM

- Catherine Thieblemont et al.
- To describe real world treatment scenario in France

CAR T in DLBCL

- 5 authorized centres (APHP, Hôpital Saint-Louis-Paris, CHU Montpellier, CHU Nantes, CHU Lyon, CHU Lille).
- 60 patients, Yescarta (30) or Kymriah (30), Median age was 52 (range 18 -77). 11 (18%) pts were over 65 years old.
- 68% were primary refractory defined as progressive or stable disease as the best response to the most recent chemotherapy. Median number of prior lines was 3 (range 2 to 9) and 18 (30%) pts had a prior ASCT

➢ **time duration between the ATU validation and receipt of the CD19 CAR T-cells was 47.5 days (range 30-190 days). During this time, all patients except 4 (93%) received a bridging therapy**

Kapitel 3

CAR-T-Zellen auch für ältere Patienten?

CAR T in DLBCL: impact of age?

PS1066

AXICABTAGENE CILOLEUCEL (AXI-CEL) IN REFRACTORY LARGE B CELL LYMPHOMA: OUTCOMES IN PATIENTS ≥ OR < 65 YEARS OF AGE IN THE PIVOTAL PHASE 1/2 ZUMA-1 STUDY

- Sattva S. Neelapu et al.
- To assess efficacy and safety outcomes of axi-cel in patients ≥ or < 65 years of age from ZUMA-1.

CAR T in DLBCL

- 108 patients were treated. Patients ≥ 65 years (n = 27) vs < 65 years (n = 81) had a median age of 69 years vs 55 years.
- Comparable characteristics in terms of IPI; prior regimens, ECOG PS, and tumor burden
- The objective ORR for patients ≥ 65 years (n = 24) and < 65 years (n = 77) was 92% and 81% (complete response rate, 75% and 53%), respectively,
- with ongoing responses in 42% and 38% of patients (ongoing complete response, 42% and 35%).
- The 24-month overall survival rate was 54% for patients ≥ 65 years and 49% for patients < 65 years.

➢ **high rates of durable responses with a manageable safety profile for patients ≥ and < 65 years**

Kapitel 4

CAR-T-Zellen bei Patienten mit sekundärem ZNS-Befall

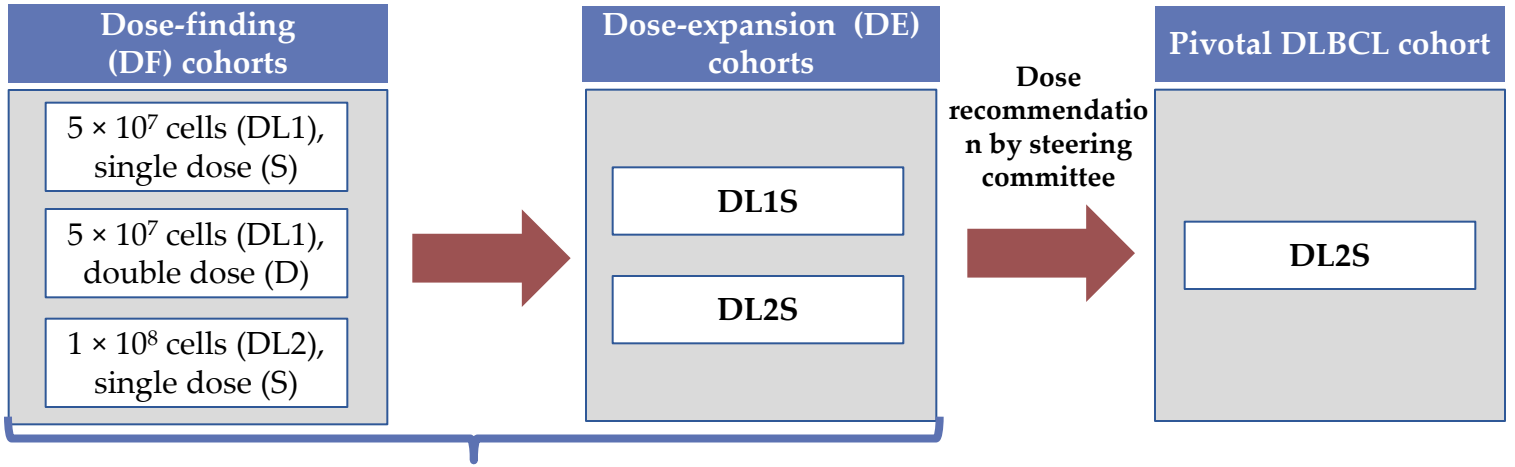
CAR T in DLBCL: CNS disease?

PF298

LISOCABTAGENE MARALEUCEL TREATMENT OF PATIENTS WITH RELAPSED/REFRACTORY B-CELL NON-HODGKIN LYMPHOMA AND SECONDARY CENTRAL NERVOUS SYSTEM LYMPHOMA: INITIAL RESULTS FROM TRANSCEND NHL 001

- Jeremy Abramson et al.
- To assess efficacy of LISOCABTAGENE MARALEUCEL in patients with aggressive lymphoma and secondary CNS disease in the phase 1 TRANSCEND NHL 001 study

TRANSCEND-NHL-001: multicenter, seamless design pivotal trial of lisocabtagene maraleucel in R/R DLBCL



CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; FL3b, follicular lymphoma grade 3B; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; NOS, not otherwise specified; PMBCL, primary mediastinal large B-cell lymphoma; R/R, relapsed/refractory; tFL, transformed FL.

NCT02631044. Available from: https://clinicaltrials.gov/ct2/show/NCT02631044 Abramson JS, et al. Presented at EHA 2018;abstract S800.

CAR T in DLBCL

- 9 patients with secondary CNS lymphoma at initial treatment (n=6), retreatment (n=2), or cycle 2 (n=1) received liso-cel.
- Four patients were treated at dose level 1 and 5 at dose level 2. The median (range) age was 60 (47–73) years and the number of prior lines of therapy was 3 (2–7).
- One of 9 patients had grade 2 cytokine release syndrome (CRS) and 1 of 9 patients had a neurological event (NE; grade 3 decreased level of consciousness).
- Four patients responded to liso-cel; all with a best response of complete response, of which 2 are ongoing at 270 and 545 days post-liso-cel.

➢ **Liso-cel could be safely delivered to patients with R/R B-cell NHL, including those with secondary CNS lymphoma and shows efficacy**

Kapitel 5

Anwendung auch bei anderen B-Zell-Lymphomen?

CAR T beyond DLBCL: CLL?

S109

TRANSCEND CLL 004: MINIMAL RESIDUAL DISEASE NEGATIVE RESPONSES AFTER LISOCABTAGENE MARALEUCEL (LISO-CEL) IN PATIENTS WITH RELAPSED/REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA OR SMALL LYMPHOCYTIC LYMPHOMA

- Tanya Siddiqi et al.
- To assess To assess the safety, pharmacokinetics, and efficacy of lisocabtagene maraleucel in CLL

CAR T beyond DLCBL: CLL?

- 16 patients received liso-cel: n=6 in dose level 1 and n=10 in dose level 2.
- Of the patients, 75% had high-risk features (TP53 mutation, complex karyotype, or del17p); 100% had received prior ibrutinib and 50% had received prior venetoclax. Median (range) number of prior lines of therapy was 4.5 (2–11).
- The most common grade 3/4 treatment-emergent AE were cytopenias (thrombocytopenia, 75%; anemia, 69%; neutropenia, 63%; leukopenia, 56%).
- One patient had grade 3 cytokine release syndrome (CRS); 3 patients had grade 3 neurological events (NE).

CAR T beyond DLCBL: CLL?

- Best overall response rate (ORR) in 15 evaluable patients was 87% (13/15).
- Seven patients (47%) achieved complete remission with/without complete blood count recovery (CR/CRi).
- ORR at 6 mo was 83% (5/6). Undetectable MRD (uMRD) in blood was achieved in 10/15 patients (67%) by day 30, and in BM in 7/8 patients (88%). MRD-negative CRs were seen in patients who had failed both BTKi and venetoclax.

➢ **In this study of heavily pretreated patients with standard- and high-risk CLL/SLL and previous ibrutinib treatment, liso-cel-related toxicities (ie, CRS and NEs) were manageable. Phase II is ongoing.**

Kapitel 6

Zusammenfassung

Take home messages

CAR T cell therapy in aggressive Lymphoma (DLBCL)

- **Real world:** need for bridging therapy in most patients (axi-cel and Tisagenlecleucel)
- **Age?** Age is not important, neither for efficacy nor for safety (Axi-cel)
- **Secondary CNS disease?** Feasible without excess NT and with encouraging responses seen in still few patients (Liso-cel)

CAR T cell therapy in CLL

- **Phase I:** shows feasibility and MRD negative responses, phase II is ongoing (Liso-cel)

Thank you very much for your attention!

The CAR Team in Cologne

Study physicians
Hyatt Balke-Want
Philip Goedel

Study nurses / project manager
Hanna Birkholz
Mareike Tamm
Lars Pester

Apheresis Unit
Udo Holtick
Christoph Scheid

Laboratory
Hinrich Abken and coworkers

ICU physicians
Boris Böll
Matthias Kochanek
Johanna Prinz

DCLLSG
Michael Hallek
Barbara Eichhorst

Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2019

Für den Inhalt verantwortlich:

Prof. Dr. med. Peter Borchmann

Klinik I für Innere Medizin • Uniklinik Köln

Das Informationsprojekt wird unterstützt von den Firmen

AstraZeneca

Celgene

Janssen
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Diese hatten keinen Einfluss auf die Inhalte.