Kompetenznetz Maligne Lymphome

# Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien


## EHA2024 HYBRID

Kompetenznetz Maligne Lymphome

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Expert:innen berichten zu Lymphomen & Leukämien

**Prof. Dr. med. Kai Hübel**
Innere Medizin I | Uniklinik Köln

# Follikuläres Lymphom (FL)

# Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – EHA2024 HYBRID wird in Kooperation mit sieben unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

| | |
|---|---|
| **Anstellungsverhältnis, Führungsposition** | Oberarzt, Uniklinik Köln |
| **Beratungs-/ Gutachtertätigkeit** | Roche, BMS, Incyte, Recordati, AbbVie, Novartis, Gilead, Miltenyi Biotec, BeiGene, Sandoz |
| **Besitz von Geschäftsanteilen, Aktien oder Fonds** | entfällt |
| **Patent, Urheberrecht, Verkaufslizenz** | entfällt |
| **Honorare** | Roche, Incyte, Recordati, Sandoz, Novartis, BeiGene, AbbVie |
| **Finanzierung wissenschaftlicher Untersuchungen** | Roche, Gilead, Incyte |
| **Andere finanzielle Beziehungen** | entfällt |
| **Immaterielle Interessenkonflikte** | entfällt |

# Kapitel 1

Die bispezifischen Antikörper – im Zentrum des Interesses auf diesem EHA!

# MOSUNETUZUMAB DEMONSTRATES CLINICALLY MEANINGFUL OUTCOMES IN HIGH-RISK PATIENTS WITH HEAVILY PRE-TREATED R/R FL AFTER ≥3 YEARS OF FOLLOW-UP: SUBGROUP ANALYSIS OF A PIVOTAL PHASE II Study

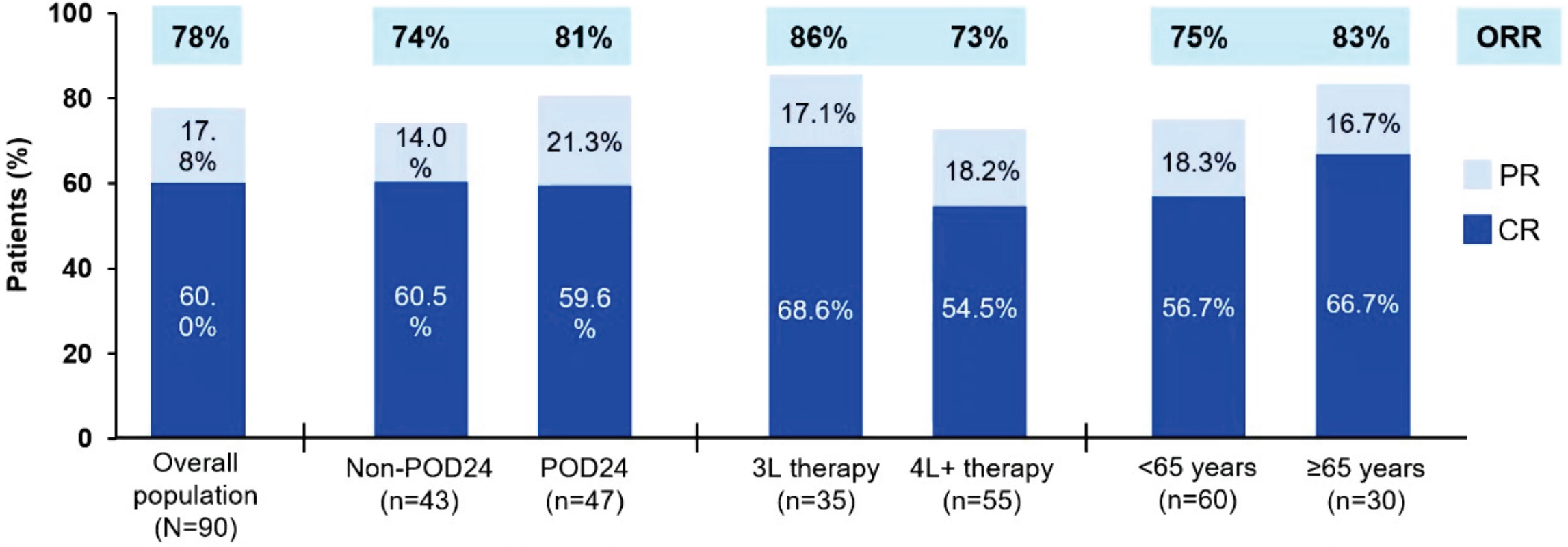
**Abstract #S233**

Sarit Assouline et al.

# Patienten-Charakteristik in den Subgruppen

| | Overall population (N=90) | POD24 status | | Line of therapy | | Age | |
|---|---|---|---|---|---|---|---|
| | | Non-POD24 (n=43) | POD24 (n=47) | 3L therapy (n=35) | 4L+ therapy (n=55) | <65 years (n=60) | ≥65 years (n=30) |
| **Median age, years (range)** | 60 (29–90) | 63 (29–90) | 57 (30–83) | 61 (29–90) | 59 (30–82) | 56 (29–64) | 71 (65–90) |
| **Male** | 55 (61%) | 22 (51%) | 33 (70%) | 17 (49%) | 38 (69%) | 41 (68%) | 14 (47%) |
| **ECOG PS** | | | | | | | |
| 0 | 53 (59%) | 24 (56%) | 29 (62%) | 19 (54%) | 34 (62%) | 36 (60%) | 17 (57%) |
| 1 | 37 (41%) | 19 (44%) | 18 (38%) | 16 (46%) | 21 (38%) | 24 (40%) | 13 (43%) |
| **Ann Arbor stage III/IV** | 69 (77%) | 29 (67%) | 40 (85%) | 25 (71%) | 44 (80%) | 48 (80%) | 21 (70%) |
| **Median lines of prior therapy, n (range)** | 3 (2–10) | 3 (2–7) | 3 (2–10) | 2 (2–2) | 4 (3–10) | 3 (2–10) | 3 (2–7) |
| **Refractory to last prior therapy** | 62 (69%) | 26 (61%) | 36 (77%) | 22 (63%) | 40 (73%) | 44 (73%) | 18 (60%) |
| **Refractory to prior anti-CD20 therapy** | 71 (79%) | 31 (72%) | 40 (85%) | 25 (71%) | 46 (84%) | 48 (80%) | 23 (77%) |
| **Double refractory** | 48 (53%) | 19 (44%) | 29 (62%) | 13 (37%) | 35 (64%) | 35 (58%) | 13 (43%) |

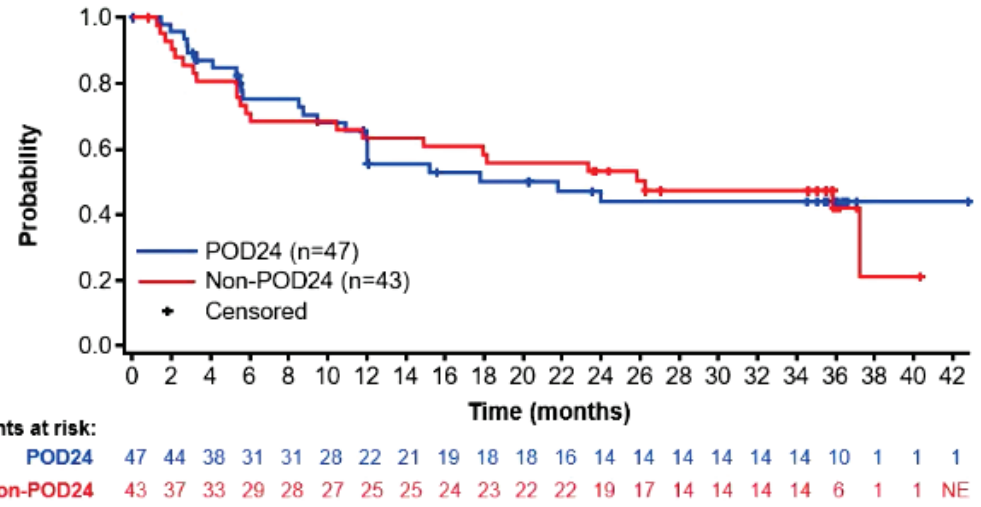
# Therapieansprechen




**CR rates across high-risk subgroups were consistent with the overall population; higher CR rates were observed in patients who received mosunetuzumab in 3L than in the other subgroups**

# Subgruppe POD24

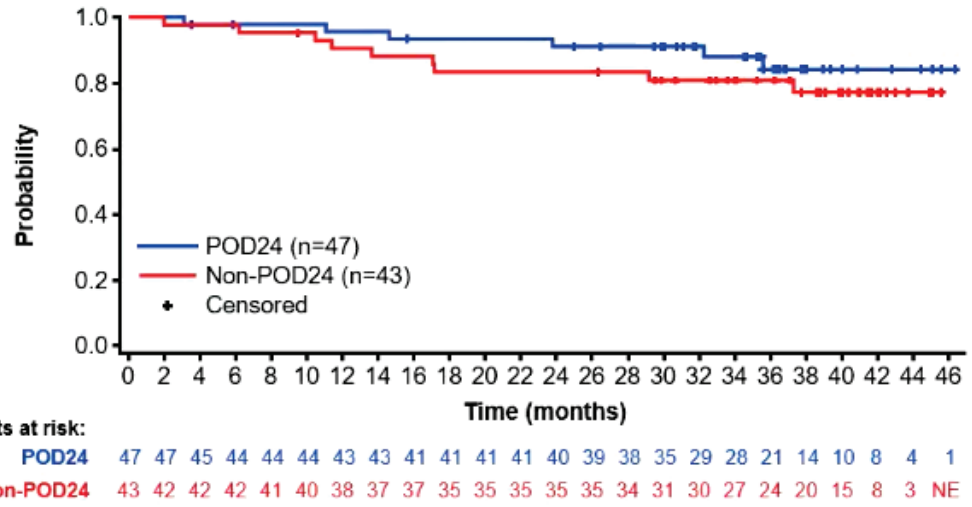
## PFS




Patients at risk:

| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| POD24 | 47 | 44 | 38 | 31 | 31 | 28 | 22 | 21 | 19 | 18 | 18 | 16 | 14 | 14 | 14 | 14 | 14 | 14 | 10 | 1 | 1 | 1 |
| Non-POD24 | 43 | 37 | 33 | 29 | 28 | 27 | 25 | 25 | 24 | 23 | 22 | 22 | 19 | 17 | 14 | 14 | 14 | 14 | 6 | 1 | 1 | NE |

## OS




Patients at risk:

| | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| POD24 | 47 | 47 | 45 | 44 | 44 | 44 | 43 | 43 | 41 | 41 | 41 | 41 | 40 | 39 | 38 | 35 | 29 | 28 | 21 | 14 | 10 | 8 | 4 | 1 |
| Non-POD24 | 43 | 42 | 42 | 42 | 41 | 40 | 38 | 37 | 37 | 35 | 35 | 35 | 35 | 35 | 34 | 31 | 30 | 27 | 24 | 20 | 15 | 8 | 3 | NE |

| | Overall population (N=90) | Non-POD24 (n=43) | POD24 (n=47) |
|---|---|---|---|
| **Median PFS,** months (95% CI) | 24.0 (12.0–NE) | 26.3 (11.8–NE) | 17.8 (12.0–NE) |
| **36-month PFS,** % (95% CI) | 43 (31.8–54.7) | 42 (25.0–59.0) | 44 (28.2–59.5) |

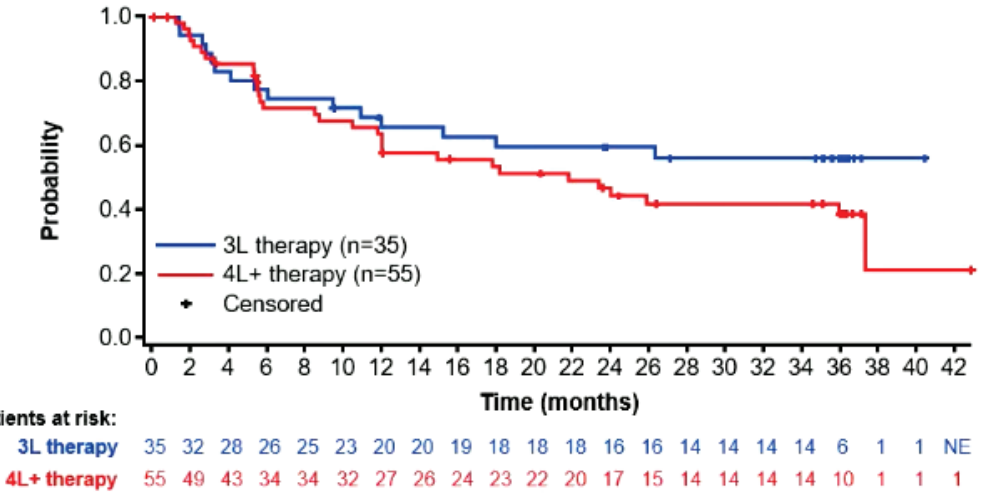
| | Overall population (N=90) | Non-POD24 (n=43) | POD24 (n=47) |
|---|---|---|---|
| **Median OS,** months (95% CI) | NR (NE) | NR (NE) | NR (NE) |
| **36-month OS,** % (95% CI) | 83 (74.6–91.2) | 81 (69.1–92.9) | 84 (72.1–96.3) |

**Similar PFS and OS benefit were observed in patients with non-POD24 and POD24**

PFS, progression-free survival.

# Subgruppe Therapielinie

## PFS

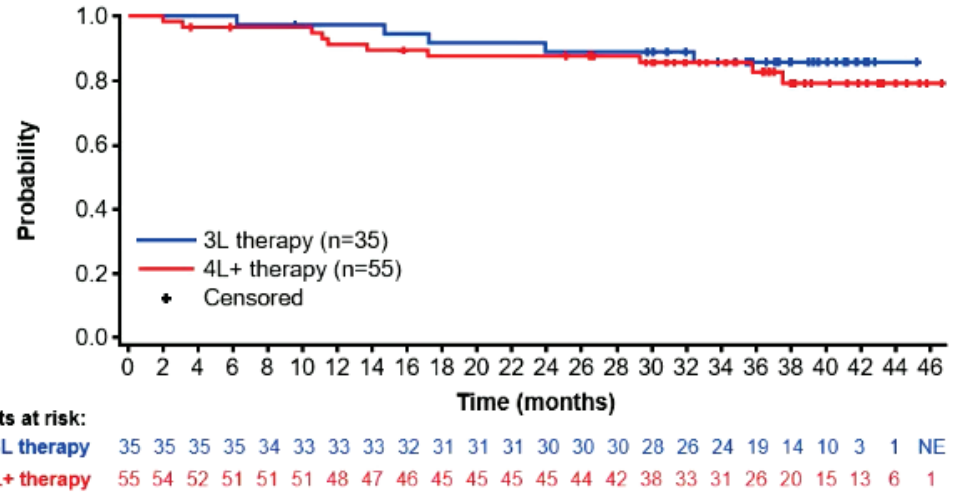



Patients at risk:

| | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3L therapy | 35 | 32 | 28 | 26 | 25 | 23 | 20 | 20 | 19 | 18 | 18 | 18 | 16 | 16 | 14 | 14 | 14 | 14 | 6 | 1 | 1 | NE |
| 4L+ therapy | 55 | 49 | 43 | 34 | 34 | 32 | 27 | 26 | 24 | 23 | 22 | 20 | 17 | 15 | 14 | 14 | 14 | 14 | 10 | 1 | 1 | 1 |

| | Overall population (N=90) | 3L therapy (n=35) | 4L+ therapy (n=55) |
|---|---|---|---|
| **Median PFS,** months (95% CI) | 24.0 (12.0–NE) | NR (12.0–NE) | 18.1 (11.8–37.3) |
| **36-month PFS,** % (95% CI) | 43 (31.8–54.7) | 54 (37.0–71.5) | 36 (21.8–50.7) |

## OS




Patients at risk:

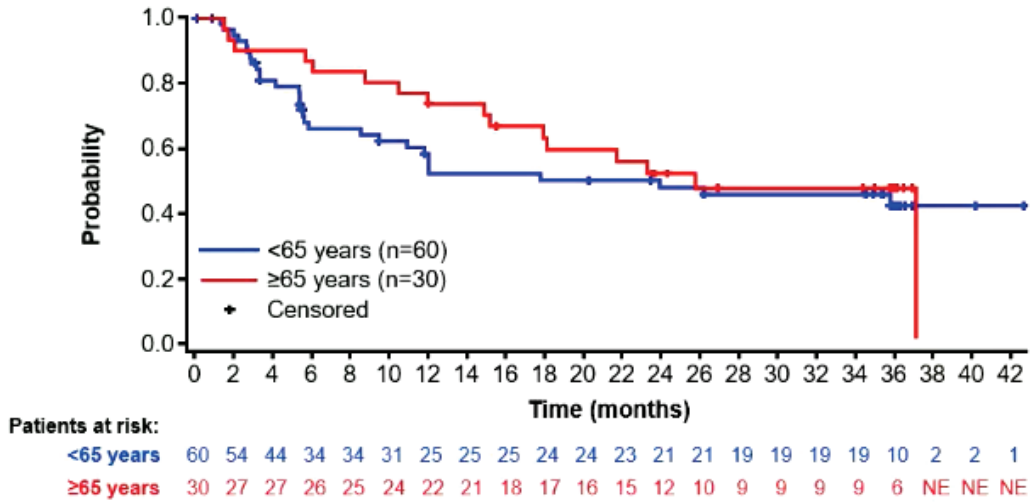
| | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3L therapy | 35 | 35 | 35 | 35 | 34 | 33 | 33 | 33 | 32 | 31 | 31 | 31 | 30 | 30 | 30 | 28 | 26 | 24 | 19 | 14 | 10 | 3 | 1 | NE |
| 4L+ therapy | 55 | 54 | 52 | 51 | 51 | 51 | 48 | 47 | 46 | 45 | 45 | 45 | 45 | 44 | 42 | 38 | 33 | 31 | 26 | 20 | 15 | 13 | 6 | 1 |

| | Overall population (N=90) | 3L therapy (n=35) | 4L+ therapy (n=55) |
|---|---|---|---|
| **Median OS,** months (95% CI) | NR (NE) | NR (NE) | NR (NE) |
| **36-month OS,** % (95% CI) | 83 (74.6–91.2) | 85 (72.7–97.2) | 82 (70.5–92.8) |

**Numerically higher PFS benefit in patients who received mosunetuzumab in 3L versus 4L+**

# Subgruppe Alter

## PFS

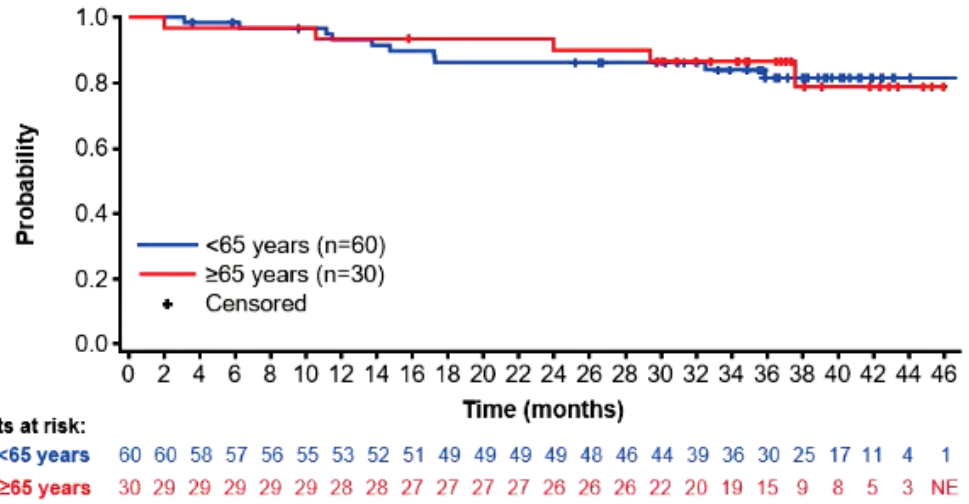



Patients at risk:

| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| <65 years | 60 | 54 | 44 | 34 | 34 | 31 | 25 | 25 | 25 | 24 | 24 | 23 | 21 | 21 | 19 | 19 | 19 | 19 | 10 | 2 | 2 | 1 |
| ≥65 years | 30 | 27 | 27 | 26 | 25 | 24 | 22 | 21 | 18 | 17 | 16 | 15 | 12 | 10 | 9 | 9 | 9 | 9 | 6 | NE | NE | NE |

| | Overall population (N=90) | <65 years (n=60) | ≥65 years (n=30) |
|---|---|---|---|
| **Median PFS,** months (95% CI) | 24.0 (12.0–NE) | 17.8 (9.4–NE) | 25.8 (15.2–NE) |
| **36-month PFS,** % (95% CI) | 43 (31.8–54.7) | 42 (27.3–55.8) | 47 (28.1–65.8) |

## OS




Patients at risk:

| | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| <65 years | 60 | 60 | 58 | 57 | 56 | 55 | 53 | 52 | 51 | 49 | 49 | 49 | 49 | 48 | 46 | 44 | 39 | 36 | 30 | 25 | 17 | 11 | 4 | 1 |
| ≥65 years | 30 | 29 | 29 | 29 | 29 | 29 | 28 | 28 | 27 | 27 | 27 | 27 | 26 | 26 | 26 | 22 | 20 | 19 | 15 | 9 | 8 | 5 | 3 | NE |

| | Overall population (N=90) | <65 years (n=60) | ≥65 years (n=30) |
|---|---|---|---|
| **Median OS,** months (95% CI) | NR (NE) | NR (NE) | NR (NE) |
| **36-month OS,** % (95% CI) | 83 (74.6–91.2) | 81 (70.6–91.9) | 86 (74.0–98.8) |

**36-month PFS and OS rates in patients ≥65 years were consistent with the overall population**

# EPCORITAMAB INDUCES DEEP RESPONSES IN RELAPSED OR REFRACTORY (R/R) FOLLICULAR LYMPHOMA (FL): SAFETY AND POOLED EFFICACY DATA FROM EPCORE NHL-1 PIVOTAL AND CYCLE (C) 1 OPTIMIZATION (OPT) FL COHORTS

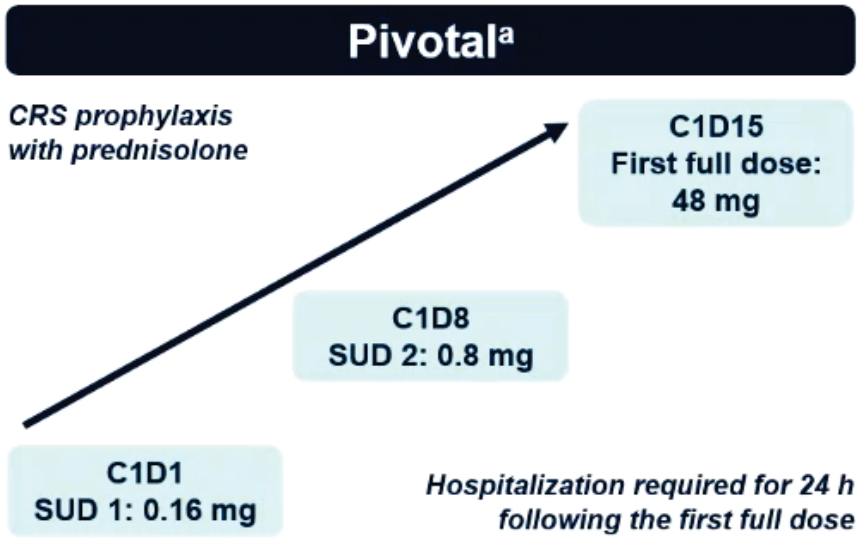
**Abstract #S234**

Umberto Vitolo et al.

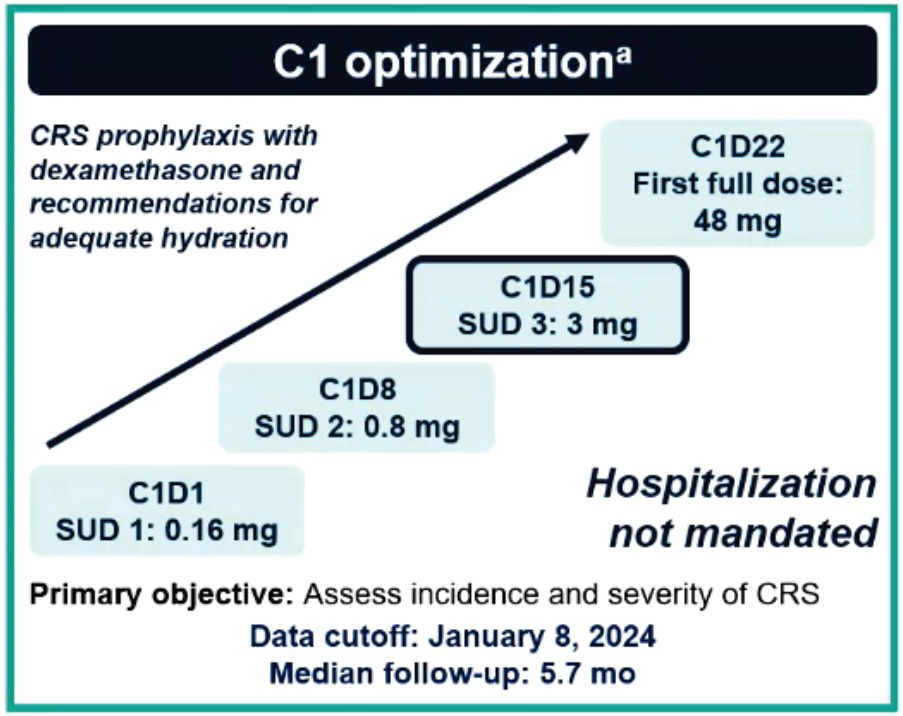
# EPCORE NHL-1: Studiendesign

**Key inclusion criteria**

- R/R CD20+ FL grade 1–3A
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 regimen with an anti-CD20 mAb
- Prior treatment with an alkylating agent or lenalidomide
- FDG-avid disease by PET/CT
- Prior CAR T allowed




N=128




N=86

Phase 1/2 trial. C, cycle; CAR T, chimeric antigen receptor T-cell therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; mAb, monoclonal antibody; MRD, minimum residual disease; OPT, optimization; ORR, overall response rate; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SUD, step-up dose. [a]Patients received subcutaneous epcoritamab QW C1–3, Q2W C4–9, and Q4W C≥10 until progressive disease (≥2 measurable [by CT/MRI] and FDG PET–positive lesions) or unacceptable toxicity. Radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. MRD was assessed in peripheral blood using the clonoSEQ® (Adaptive Biotechnologies, Seattle, WA) next-generation sequencing assay. ClinicalTrials.gov: NCT03625037; EudraCT: 2017-001748-36.

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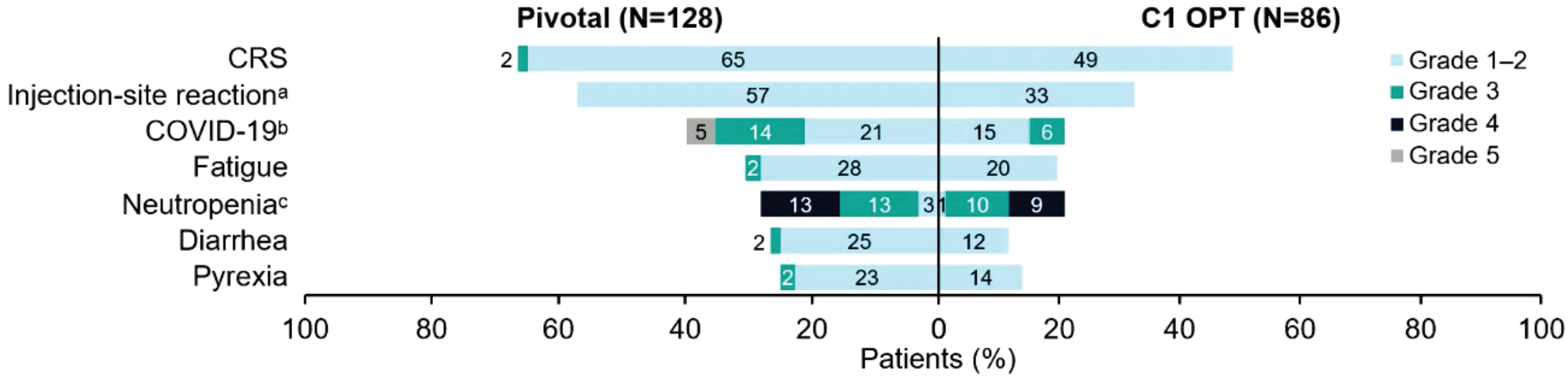
# EPCORE NHL-1: Toxizitäten




- In the C1 OPT cohort:
  - Grade ≥3 TEAEs occurred in 46 patients (53%)
  - TEAEs led to treatment discontinuation in 3 patients (3%; grade 2 bronchopulmonary aspergillosis [n=1] and pneumonitis [n=2])
  - No fatal TEAEs
- No clinical tumor lysis syndrome occurred in either cohort
- There is an increased risk of morbidity and mortality due to infections for patients with hematologic malignancies being treated with B-cell–depleting therapies

Graph shows TEAEs that occurred in ≥25% of patients in either cohort. TEAE, treatment-emergent AE. [a]Combined term includes injection-site reaction, erythema, rash, bruising, pruritus, inflammation, pain, edema, and nodule. [b]Combined term includes COVID-19 and COVID-19 pneumonia. [c]Combined term includes neutropenia and neutrophil count decreased. Four patients in the pivotal cohort and 1 patient in C1 OPT had febrile neutropenia (all grade 3).

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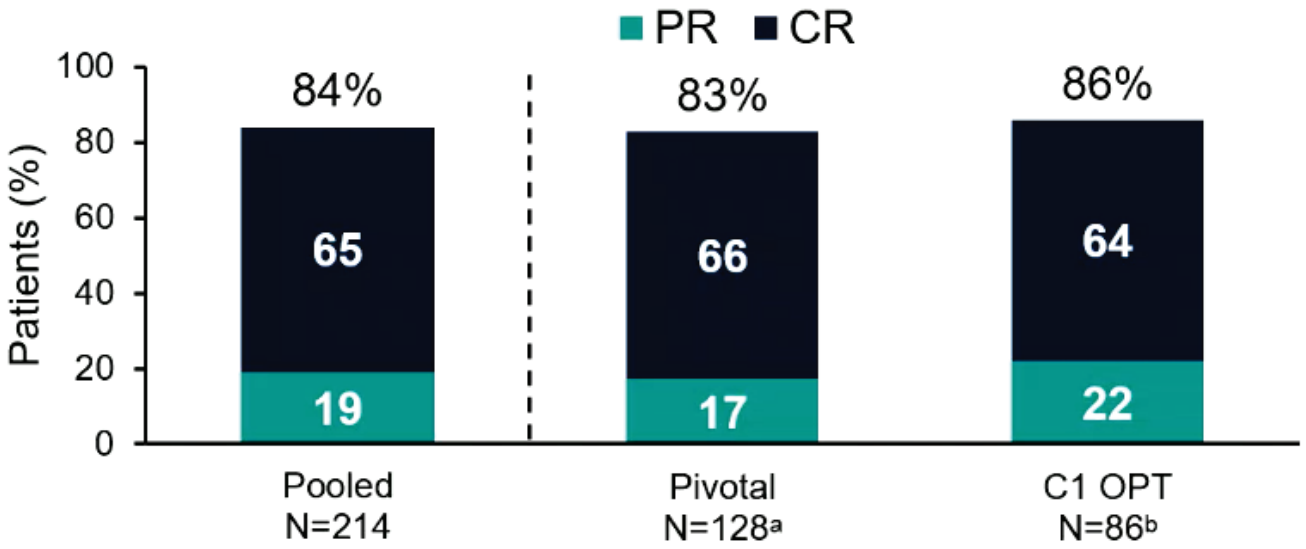
# EPCORE NHL-1: Therapieansprechen / MRD




| MRD-Negativity Rate | n (%) |
|---|---|
| Pooled (n=135) | 89 (66) |
| Pivotal (n=91) | 61 (67) |
| C1 OPT (n=44) | 28 (64) |

Based on MRD-evaluable population per clonoSEQ® PBMC assay with $10^{-6}$ cutoff.

- No impact on time to response in C1 OPT
  - Median time to response was 1.4 mo in both cohorts[c]
  - Median time to complete response was 1.5 mo in both cohorts[d]

CR was complete metabolic response (ie, PET negativity). CR, complete response; PBMC, peripheral blood mononuclear cell; PR, partial response. [a]Three patients (2%) were not evaluable. [b]Five patients (6%) were not evaluable. [c]Range: 1.2–4.4 in C1 OPT, 1.0–3.0 in pivotal. [d]Range: 1.2–4.7 in C1 OPT, 1.2–11.1 in pivotal.

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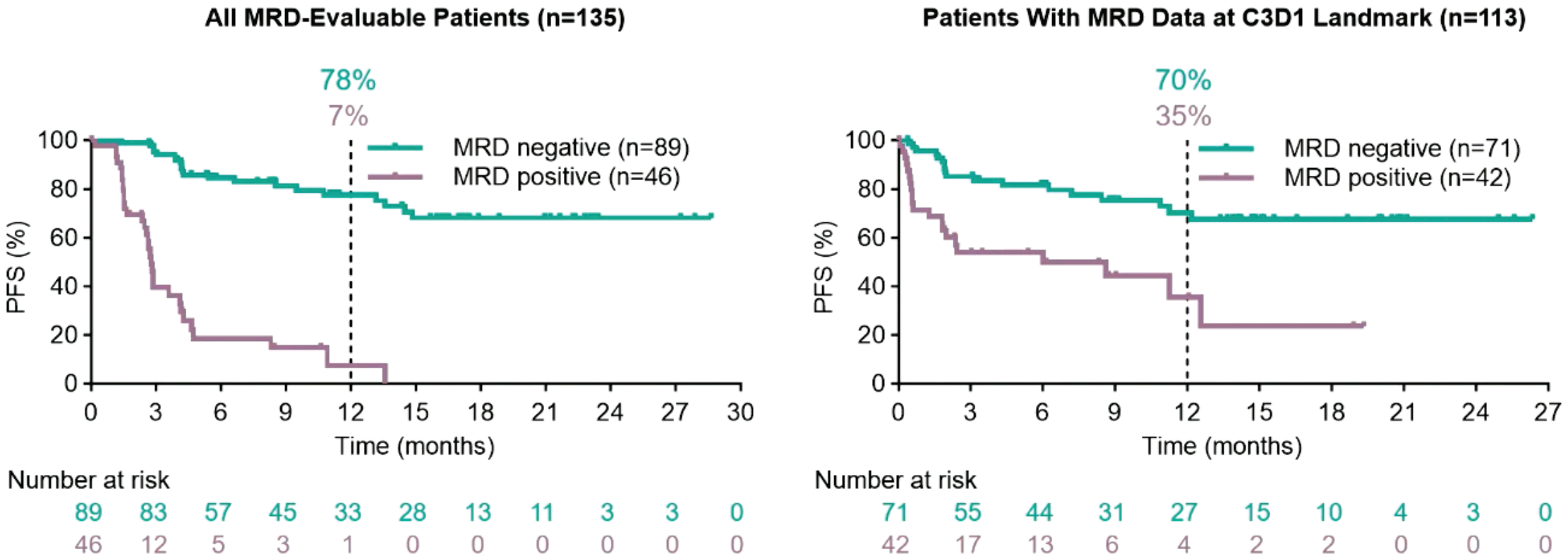
# EPCORE NHL-1: MRD-Negativität und PFS




Median follow-up: 17.4 mo for pivotal cohort and 5.7 mo for C1 OPT cohort. PFS assessed by investigator. MRD was assessed in peripheral blood using the clonoSEQ® next-generation sequencing assay with $10^{-6}$ cutoff. MRD negative was defined as having MRD negativity at any time point (left graph) or at any time point up to C3D1 (right graph).

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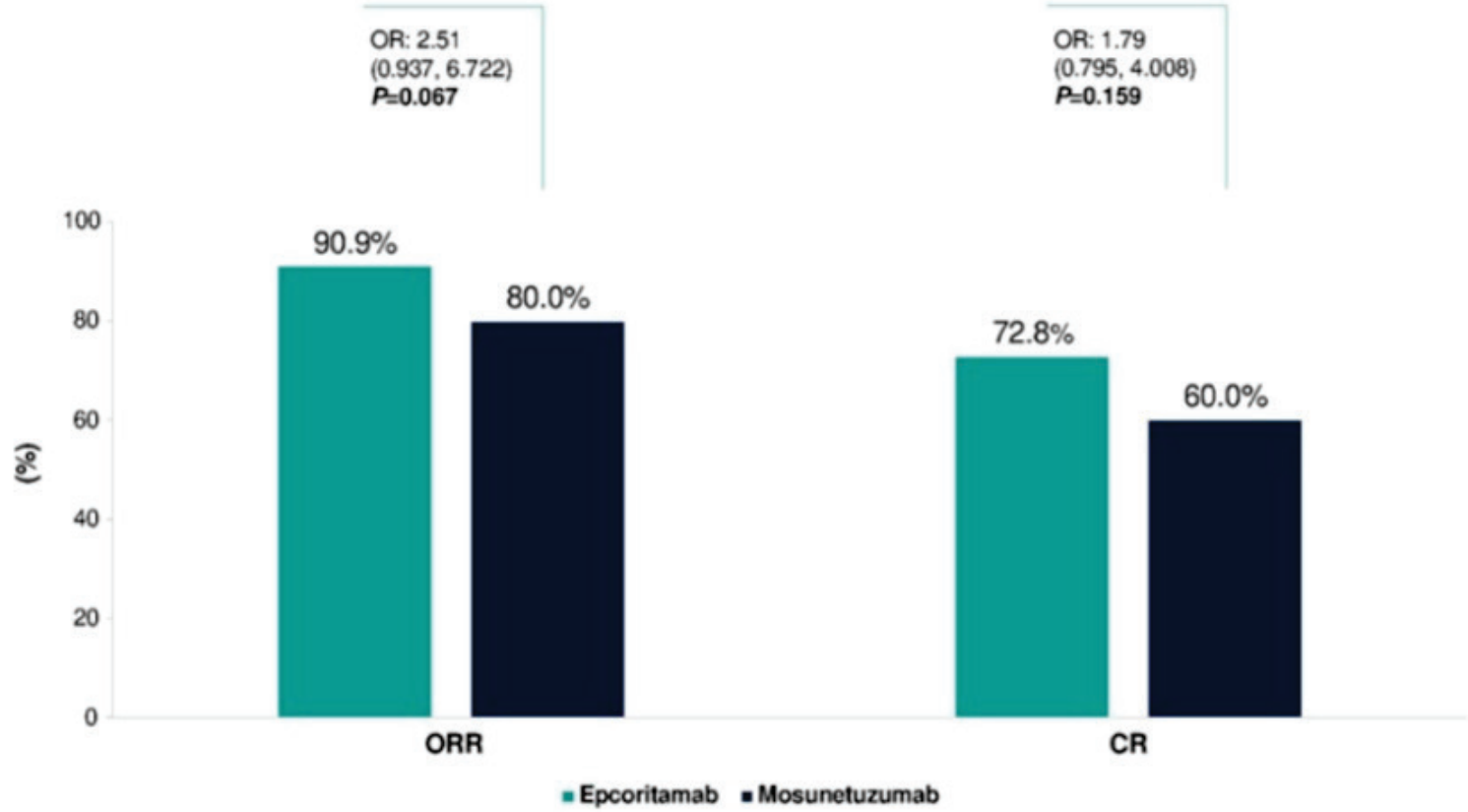
# MATCHING-ADJUSTED INDIRECT COMPARISONS OF EPCORITAMAB VS MOSUNETUZUMAB OR ODRONEXTAMAB IN RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA AFTER ≥2 SYSTEMIC THERAPIES

**Abstract #P1121**

Alexey Danilov et al.

# Therapieansprechen

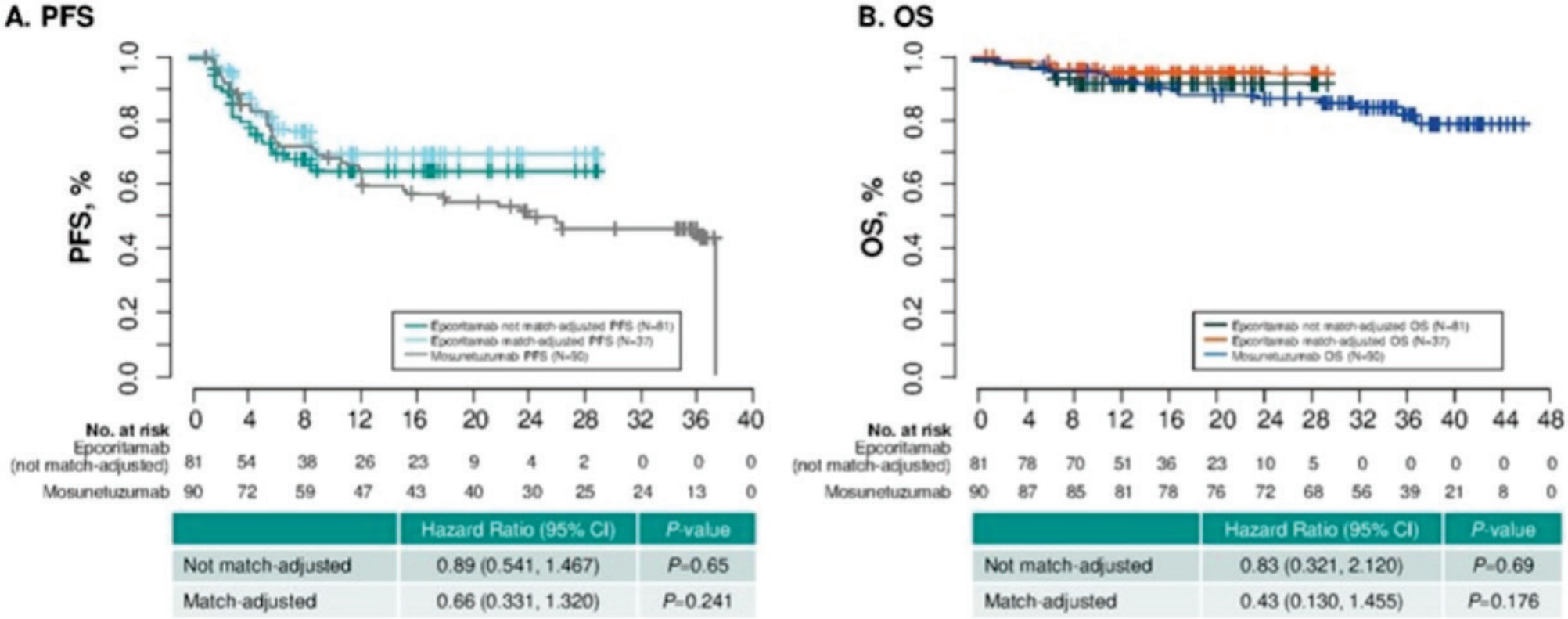
***Figure 1. Match-adjusted ORR and CR rates with odds ratios (95% CI) for epcoritamab vs mosunetuzumab***




CI, confidence interval; CR, complete response; OR, odds ratio; ORR, overall response rate.

# Therapieverlauf

## *Figure 3. PFS and OS of epcoritamab vs mosunetuzumab[a]*



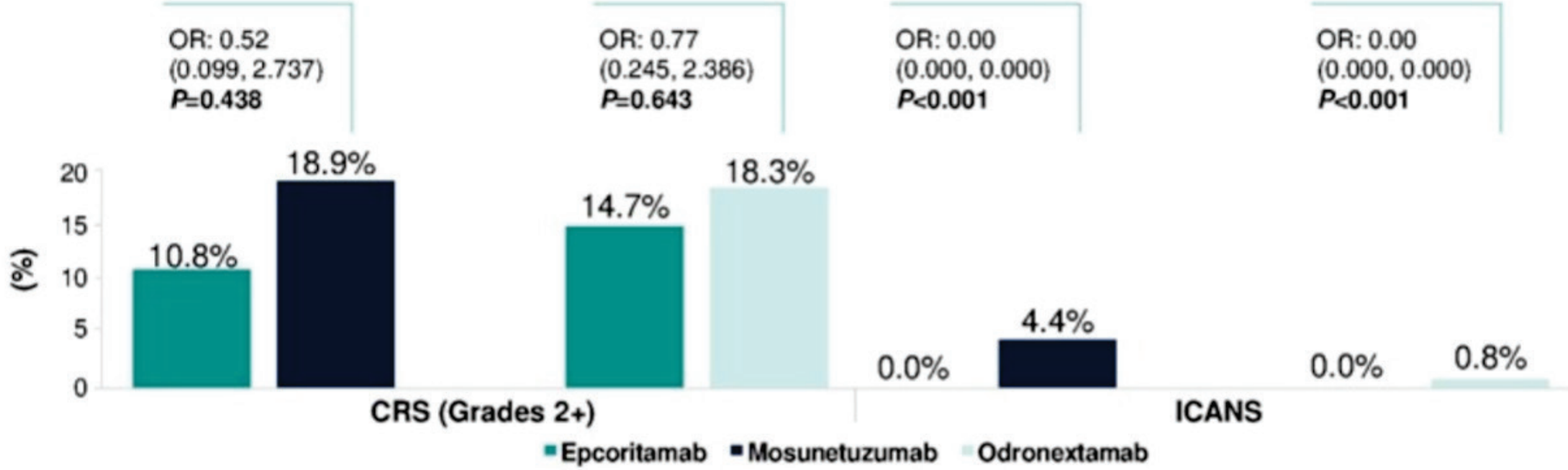

| | Hazard Ratio (95% CI) | *P*-value |
|---|---|---|
| Not match-adjusted | 0.89 (0.541, 1.467) | *P*=0.65 |
| Match-adjusted | 0.66 (0.331, 1.320) | *P*=0.241 |

| | Hazard Ratio (95% CI) | *P*-value |
|---|---|---|
| Not match-adjusted | 0.83 (0.321, 2.120) | *P*=0.69 |
| Match-adjusted | 0.43 (0.130, 1.455) | *P*=0.176 |

MAIC, matching-adjusted indirect comparison; OS, overall survival; PFS, progression-free survival.
[a]Survival analyses were adjusted for the impact of the COVID-19 pandemic by censoring COVID-19 deaths occurring during EPCORE NHL-1 data collection.

# CRS und ICANS

***Figure 5. Matching-adjusted safety comparisons for epcoritamab vs mosunetuzumab and odronextamab***




CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; OR, odds ratio.

# Kapitel 2

CAR-T-Zellen – gibt es neue Daten zum FL?

# CLINICAL OUTCOMES OF PATIENTS WITH RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA TREATED WITH TISAGENLECLEUCEL: PHASE 2 ELARA 3-YEAR FOLLOW-UP

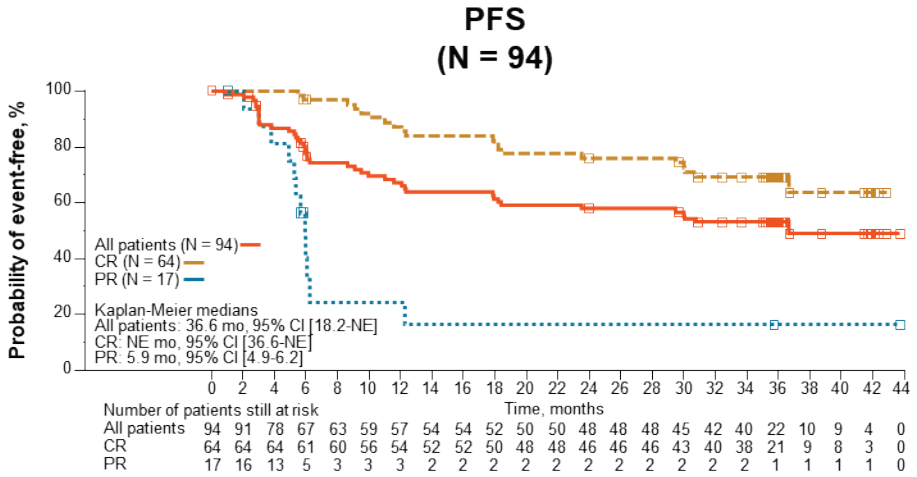
**Abstract #P1455**

Martin Dreyling et al.

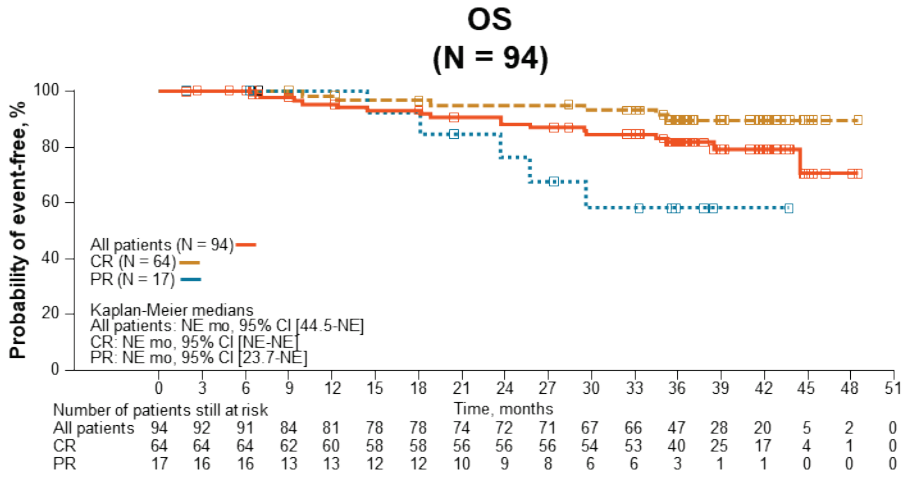
# ELARA: Patienten-Charakteristik

| | Infused set (N = 97) |
|---|---|
| Median age (range), years | 57.0 (29-73) |
| ECOG PS ≥1 prior to infusion, n (%) | 42 (43) |
| Stage at study entry III-IV, n (%) | 83 (86) |
| Bone marrow involvement, n (%) | 37 (38) |
| **Bulky disease,[a] n (%)** | **62 (64)** |
| FLIPI high at study entry (≥3), n (%) | 58 (60) |
| Median no. of prior therapies (range) | 4 (2-13) |
| **POD24 from first anti-CD20 mAb containing therapy, n (%)** | **61 (63)** |
| Refractory disease to last line of therapy, n (%) | 76 (78) |
| Refractory to ≥2 regimens, n (%) | 69 (71) |
| **Double refractory: anti-CD20 mAb + alkylating agent** | **66 (68)** |
| Refractory to PI3K inhibitors | 14 (14) |
| Prior autologous HSCT, n (%) | 35 (36) |
| **Comorbidities, n (%)** | |
| **Cardiac disorders** | **15 (16)** |
| **Diabetes** | **10 (10)** |
| **Renal insufficiency** | **8 (8)** |

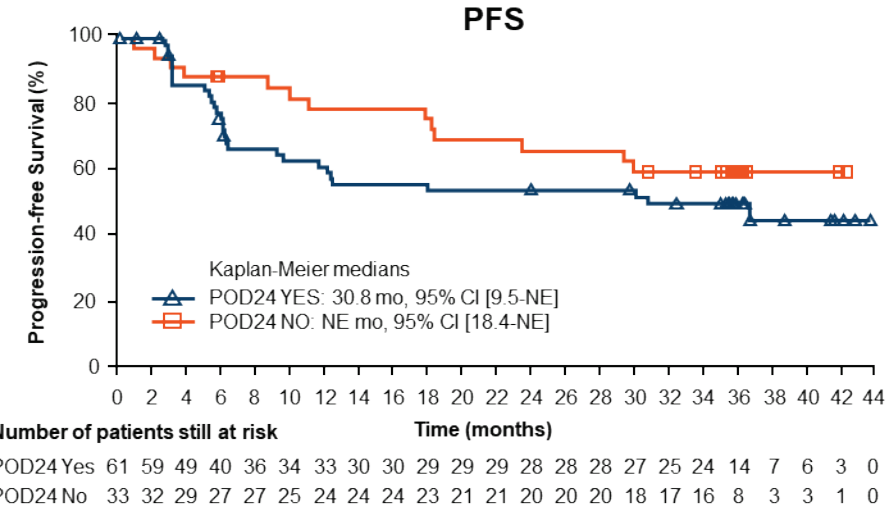
# ELARA: PFS und OS

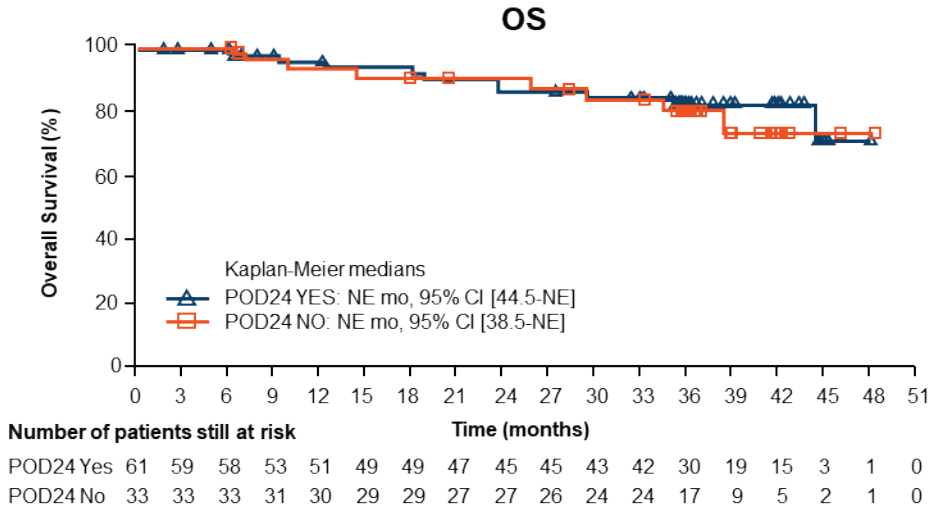



Median PFS was 37 months

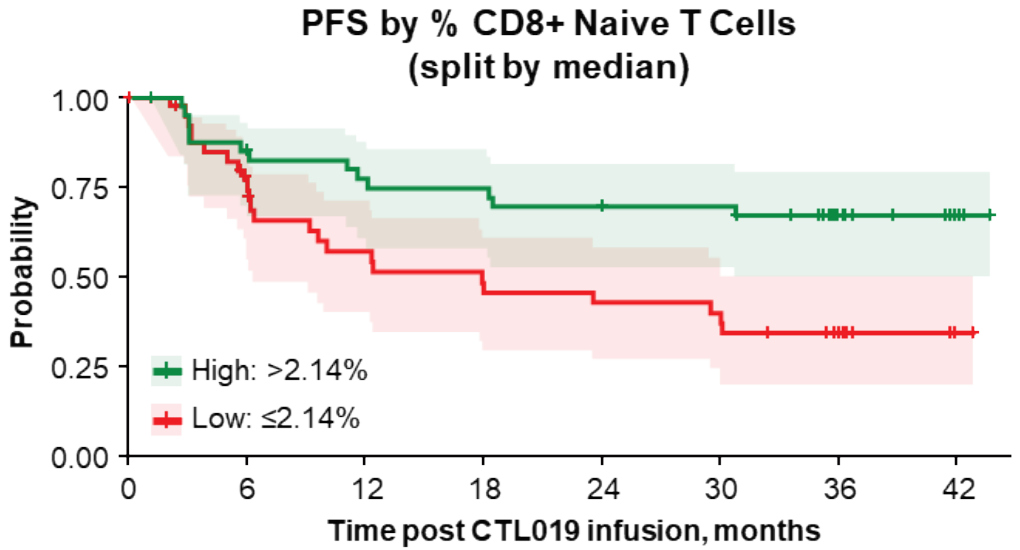



Median OS was not reached



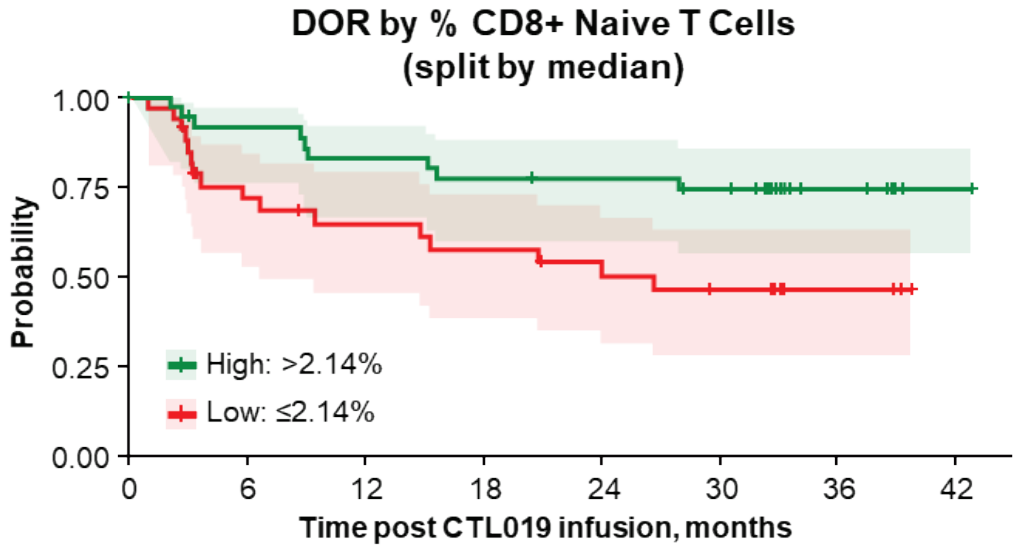



# ELARA: Biomarker-Analysen




Number at risk (number of events)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Low: ≤2.14% | 41 (0) | 26 (11) | 20 (16) | 16 (20) | 15 (21) | 13 (23) | 9 (24) | 1 (24) |
| High: >2.14% | 41 (0) | 33 (6) | 30 (9) | 29 (10) | 26 (12) | 26 (12) | 11 (13) | 3 (13) |




Number at risk (number of events)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Low: ≤2.14% | 34 (0) | 21 (9) | 18 (11) | 16 (13) | 14 (14) | 11 (16) | 3 (16) | 0 (16) |
| High: >2.14% | 37 (0) | 32 (3) | 29 (6) | 27 (8) | 26 (8) | 24 (9) | 7 (9) | 1 (9) |

# Kapitel 3

Die Transformation – kann die Prognose abgeschätzt werden?

# TIMING MATTERS: IMPACT OF EARLY HISTOLOGICAL TRANSFORMATION ON SURVIVAL IN FOLLICULAR LYMPHOMA (FL) PATIENTS: A MULTICENTRE ANALYSIS

**Abstract #P1108**

Andrea Franch et al.

# Hintergrund und Methodik

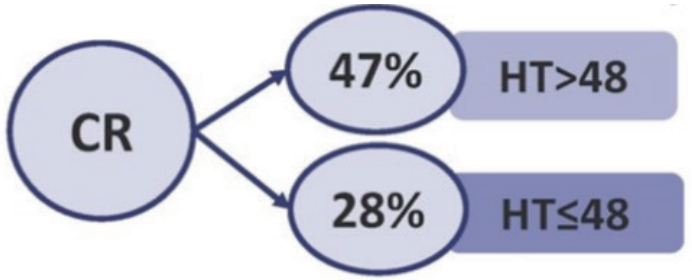
- **154 patients** (76F/78M; median age 62 years) with **FL grade 1-3a** who experienced **HT** (≥6 months after diagnosis)
- **2003 - 2017**
- **20 centers** of the GELTAMO group

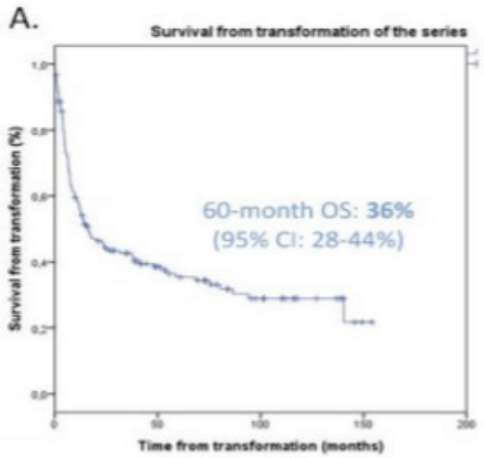
**HYSTOLOGY AT TRANSFORMATION**

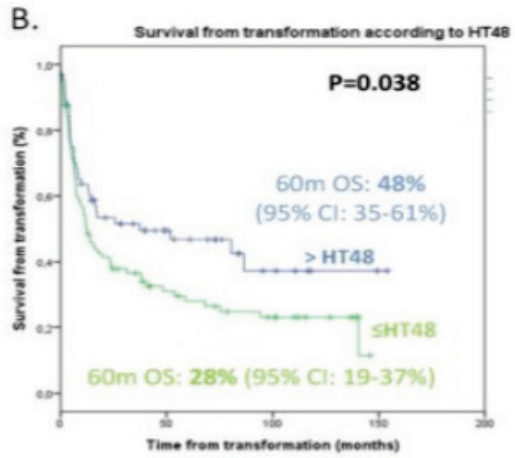

- 2 groups regarding **time from diagnosis to HT:**
  - **EARLY HT (HT≤48)** Before 48 months from diagnosis
  - **LATE HT (HT>48)** After 48 months from diagnosis
- Clinical characteristics and treatment at HT, as well as survival after HT were analyzed based on the timing of HT.

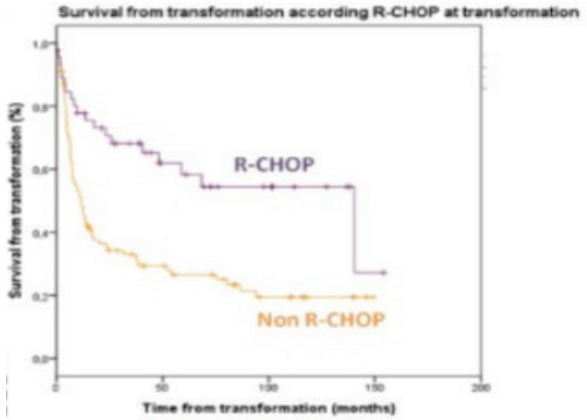
# Ergebnisse

**CR rate was lower in HT≤48** (p= 0.02).



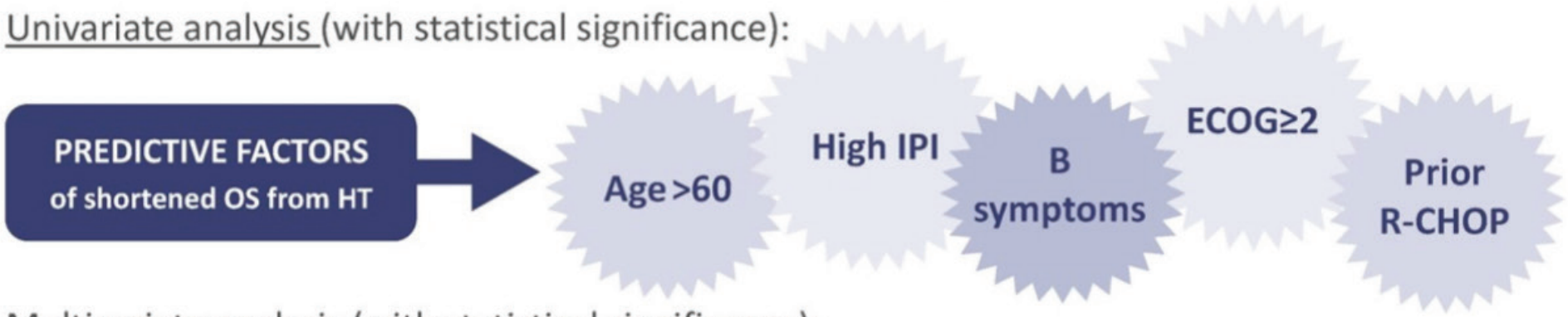



# Risikofaktoren

- Univariate analysis (with statistical significance):




- Multivariate analysis (with statistical significance):

# Zusammenfassung | Take-Home-Messages

- Die CD3xCD20 bispezifischen Antikörper zeigen eine hohe Effektivität beim r/r FL. Auch bei Risiko-Patienten (z.B. POD24) sind bispezifische Antikörper sehr gut wirksam.

- Die Nebenwirkungen (CRS, ICANS) der bispezifischen Antikörper sind beherrschbar und lassen sich durch eine Dosismodifikation zu Therapiebeginn weiter reduzieren.

- Die CAR-T-Zellen belegen im mehrjährigen Verlauf ein gutes Ansprechen bei akzeptablem Nebenwirkungsprofil.

- Patienten mit einer Transformation innerhalb von 48 Monaten nach Erstdiagnose haben ein ungünstiges Gesamtüberleben.

Die Kurzpräsentationen sind online unter

**www.lymphome.de/eha2024**

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Lymphom Kompetenz KOMPAKT

KML KONGRESSE

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