Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML-Experten berichten

63rd ASH Meeting 2021

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Lymphom Kompetenz KOMPAKT

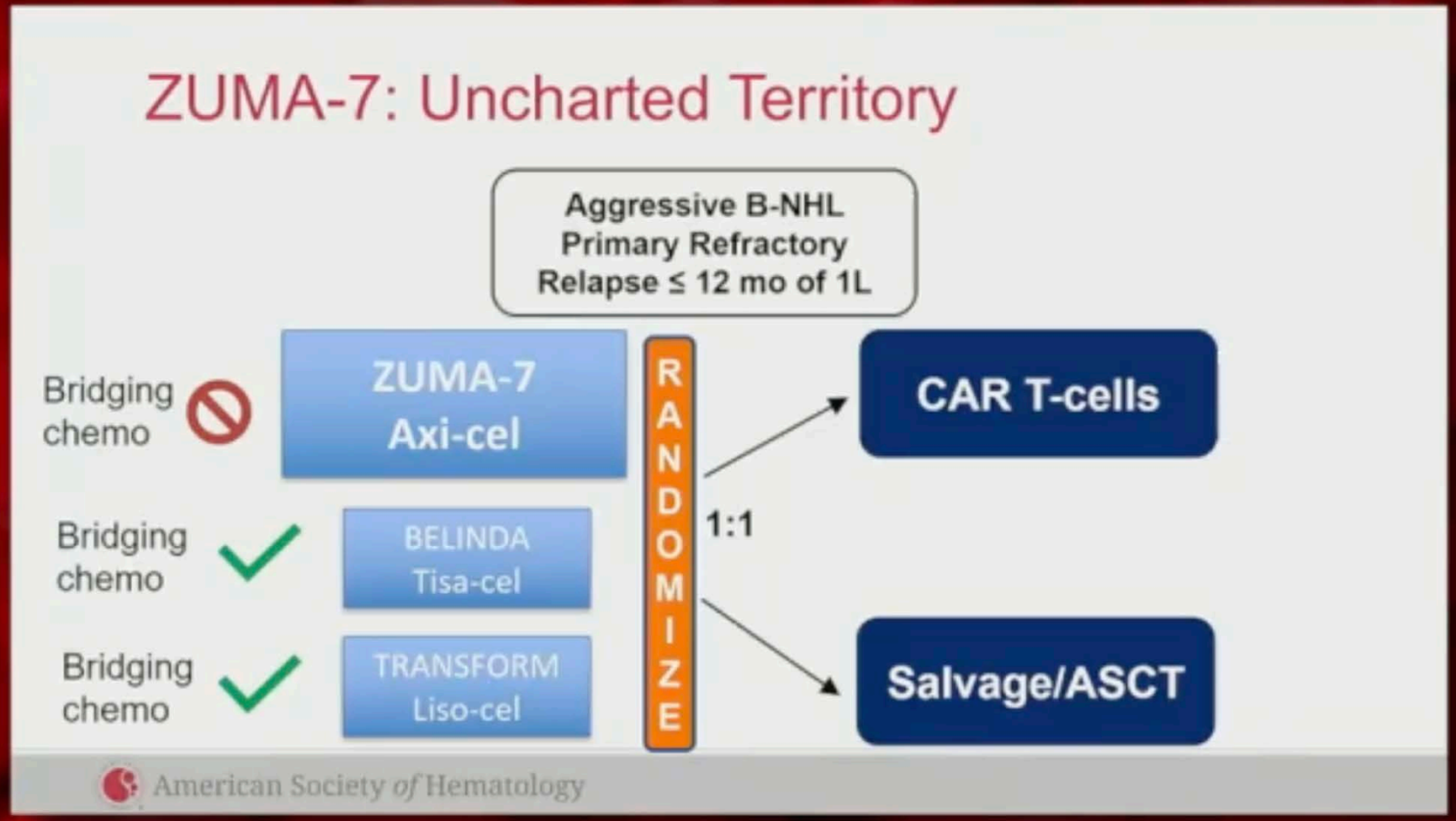
Prof. Dr. med. Michael Hallek
Klinik I für Innere Medizin | Uniklinik Köln

Grußwort

ASH 2021 | Atlanta & virtual
11. – 14. Dezember 2021

Lymphom
Kompetenz
KOMPAKT

Prof. Dr. med. Michael Hallek
Uniklinik Köln


ZUMA-7: Uncharted Territory
Aggressive B-NHL
Primary Refractory
Relapse ≤ 12 mo of 1L
Bridging chemo
ZUMA-7
Axi-cel
Bridging chemo
BELINDA
Tisa-cel
Bridging chemo
TRANSFORM
Liso-cel
RANDOMIZE
1:1
CAR T-cells
Salvage/ASCT
American Society of Hematology

Dr Nangalia

Primary Analysis of ZUMA-7: a Phase 3 Randomized Trial of Axicabtagene Ciloleucel versus Standard-of-Care Therapy in Patients with Relapsed/Refractory Large B-Cell Lymphoma

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Background

- Axi-cel is an autologous anti-CD19 CAR T-cell therapy approved for the treatment of adult patients with R/R LBCL after ≥2 lines of systemic therapy
- Current SOC second-line treatment in the curative setting for patients with R/R LBCL is salvage chemotherapy followed by consolidative HDT-ASCT[1]
- Many patients cannot receive HDT-ASCT, and their prognosis is poor[2-4]
- ZUMA-7 (NCT03391466) is the first randomized, global, multicenter Phase 3 study of axi-cel versus SOC as second-line treatment in patients with R/R LBCL

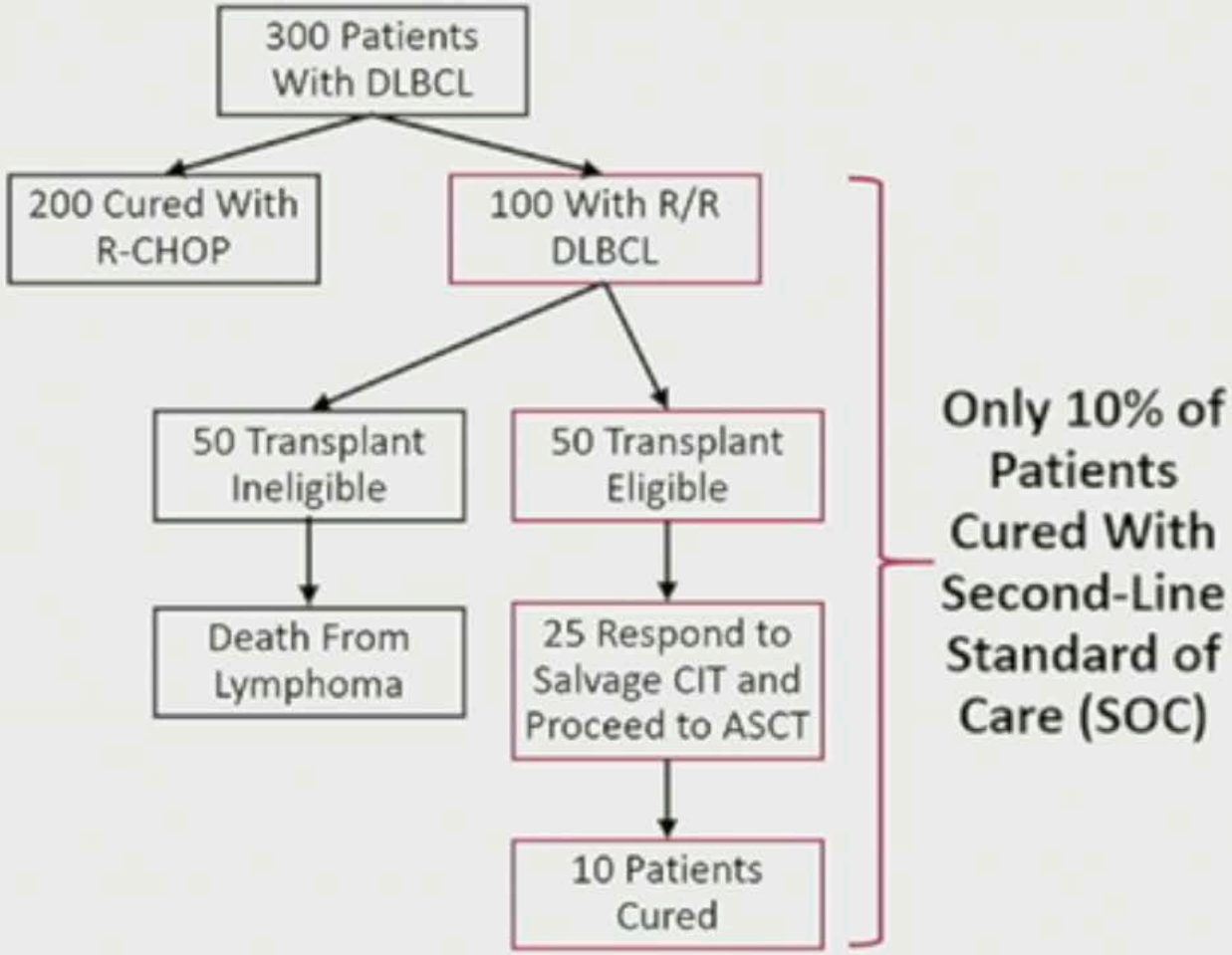


Figure adapted with permission from Friedberg. *Hematology Am Soc Hematol Educ Program*. 2011;2011:498-505.

1. Zahid U, et al. *Curr Hematol Malig Rep*. 2017;12:217-226. 2. Gisselbrecht C, et al. *J Clin Oncol*. 2010;28:4184-4190. 3. Van Den Neste E, et al. *Bone Marrow Transplant*. 2016;51:51-57. 4. van Imhoff GW, et al. *J Clin Oncol*. 2017;35:544-551.

ZUMA-7 Study Schema and Endpoints: Axi-Cel Versus SOC as Second-Line Therapy in Patients With R/R LBCL

R/R LBCL
N=359
77 sites

Key Eligibility:
- Aged ≥18 y
- LBCL[1]
- R/R ≤12 mo of 1L therapy[a]
- Intended to proceed to HDT-ASCT

Stratification:
- Response to 1L therapy
- Second-line age-adjusted IPI (sAAIPI)

Optional Steroid-Only Bridging (No Chemotherapy)

1:1 Randomization

Axi-Cel (n=180)
Conditioning Chemotherapy + Axi-cel[b]

SOC (n=179)
Cycle 1 | Cycle 2 | Cycle 3 (Optional)
Investigator-Selected Platinum-Based Chemoimmunotherapy[c]

Initial Disease Assessment (Day 50)

Responders (CR or PR)
Proceed to HDT-ASCT

Nonresponders
Additional Treatment Off Protocol[d]

Day 100 Assessment

Day 150 Assessment

LTFU Assessment

Primary Endpoint
- Event-free survival[e] (EFS) by blinded central review

Key Secondary Endpoints
- ORR
- OS

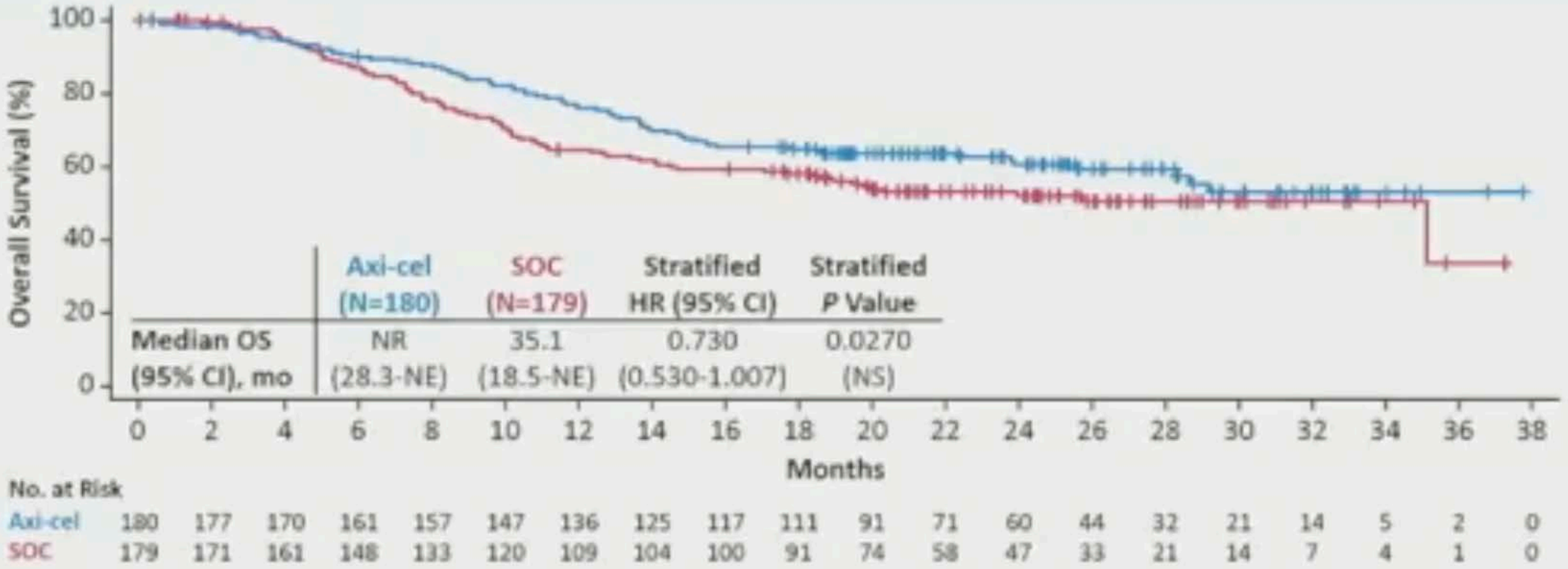
Secondary Endpoints
- PFS
- Safety
- PROs

No Protocol-Specified Crossover

[a] Refractory disease was defined as no CR to 1L therapy; relapsed disease was defined as CR followed by biopsy-proven disease relapse ≤12 months from completion of 1L therapy. [b] Axi-cel patients underwent leukapheresis followed by conditioning chemotherapy with cyclophosphamide (500 mg/m²/day) and fludarabine (30 mg/m²/day) 5, 4, and 3 days before receiving a single axi-cel infusion (target intravenous dose, 2×10^6 CAR T cells/kg). [c] Protocol-defined SOC regimens included R-GDP, R-DHAP, R-ICE, or R-ESHAP. [d] 56% of patients received subsequent cellular immunotherapy. [e] EFS was defined as time from randomization to the earliest date of disease progression per Lugano Classification,[2] commencement of new lymphoma therapy, or death from any cause.

1. Swerdlow SH, et al. *Blood*. 2016;127:2375-2390. 2. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3068.

Median OS, Evaluated as an Interim Analysis, Was Not Reached for Axi-Cel Versus 35.1 Months for SOC



- 56% of SOC patients received subsequent cellular immunotherapy (off protocol)
- Preplanned sensitivity analysis[a] suggests an OS benefit, likely confounded by SOC treatment switching

[a] Analysis utilized the validated and commonly used Rank Preserving Structural Failure Time model, which preserves randomization as described by Robins and Tsiatis (*Commun Stat Theory Methods*. 1991;2609-2631) and revealed the difference in treatment effect if SOC patients did not receive subsequent cellular immunotherapy. Stratified hazard ratio was 0.580 (95% CI, 0.416-0.809).

Post-treatment MRI is not fully accurate in anticipating cure or relapse

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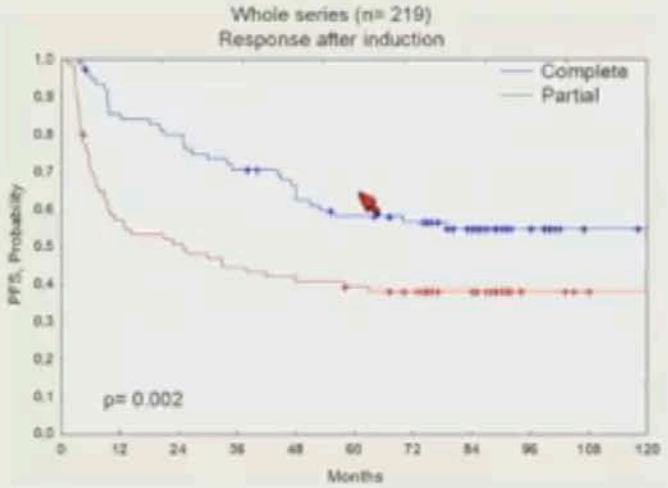
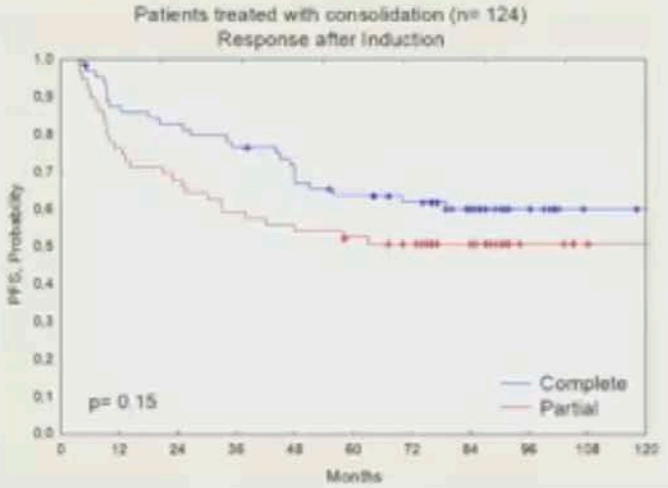
Treatment: Methotrexate-Cytarabine or Methotrexate-Cytarabine-Rituximab or Methotrexate-Cytarabine-Thiotepa-Rituximab





Some complete responders will recur some partial responders will not

(Courtesy of Prof Andrés JM Ferreri, IELSG)

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Profiling of Circulating Tumor DNA for Noninvasive Disease Detection, Risk Stratification, and MRD Monitoring in Patients with CNS Lymphoma

Mutter JA*, Alig S*, Lauer EM, Esfahani MS, Mitschke J, Kurtz DM, Kühn J, Bleul S, Olsen M, Liu CL, Jin MC, Macaulay CW, Neidert NN, Volk T, Rauer S, Heiland DH, Finke J, Duyster J, Wehrle J, Prinz M, Illerhaus G, Reinacher PC, Schorb E, Diehn M, Alizadeh AA, Scherer F

63rd ASH Annual Meeting, Plenary Session, 12/12/2021

Tumor genotyping

Biopsy-free CNSL classification

CNSL vs. Non-CNSL (other primary brain tumors or brain metastases)

- Different treatment strategies
- Suboptimal discriminatory capacity of radiographic imaging
- Mutational landscapes are fundamentally different

Hypothesis: CNSL can be diagnosed without surgical procedure based on ctDNA mutational profiles in CSF or plasma

Methodology

- Training cohort: Mutational data from 30 CNSL tumors (this study) and 2647 Non-CNSL tumors (public datasets)
- Approach: **Ensemble of Empirical Bayesian Models** to define a **Classifier score**
- Independent validation cohort: Tumor-agnostic genotyping by CAPP-Seq:
  - CNSL (35 tumors, 46 CSF, 52 plasma)
  - Non-CNSL (18 tumors, 16 CSF, 16 plasma)

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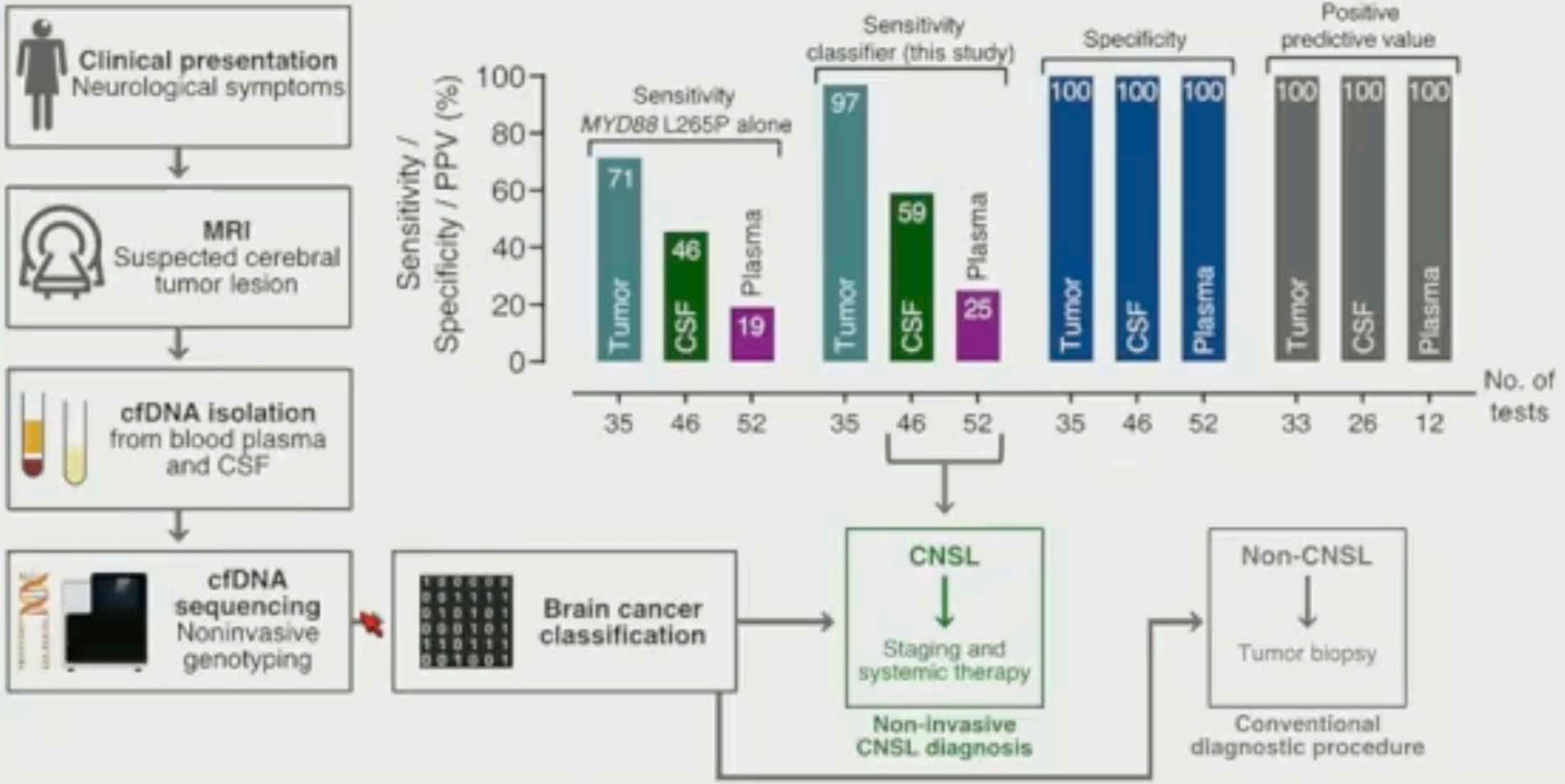
Biopsy-free CNSL classification

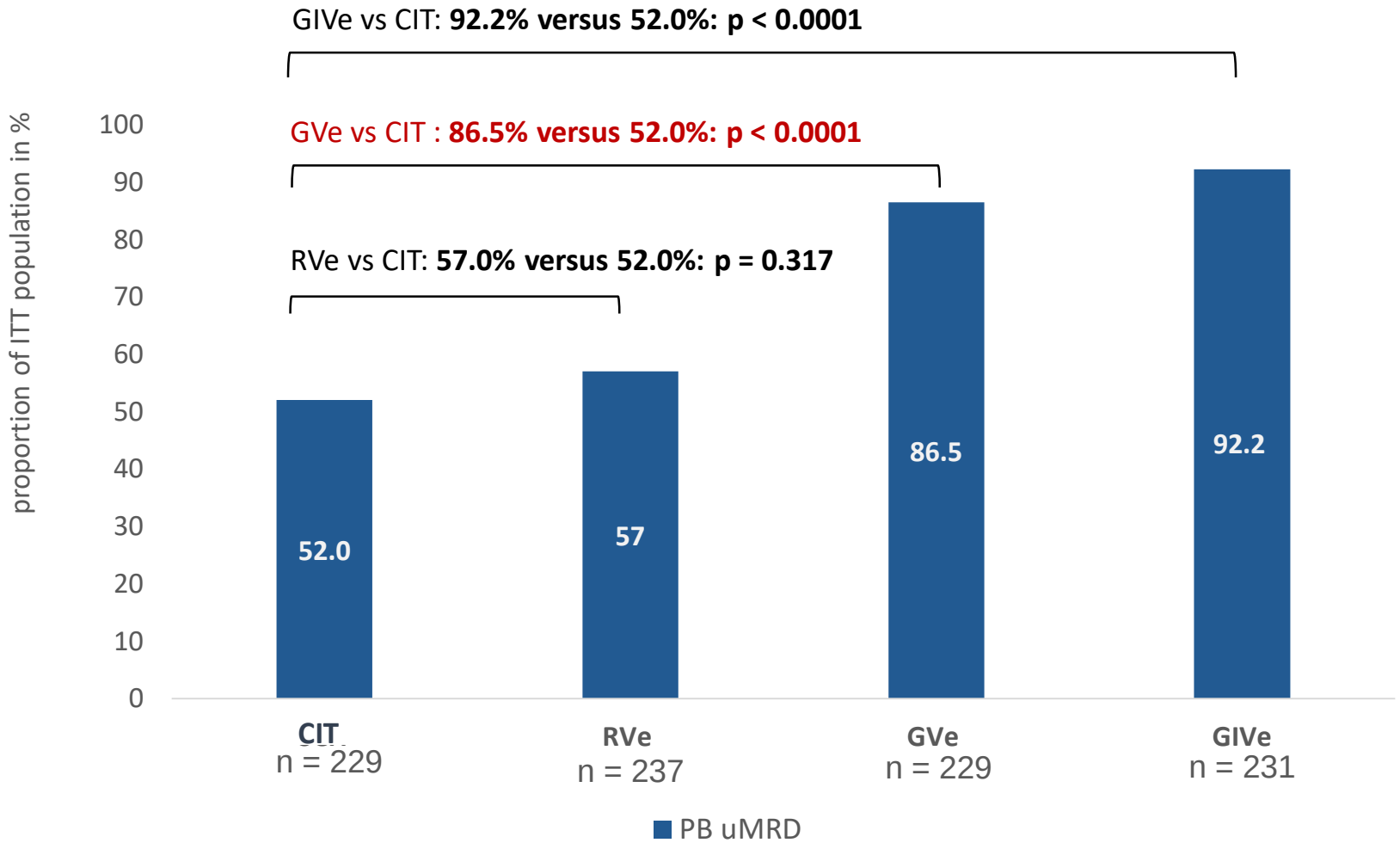


A RANDOMIZED PHASE III STUDY OF VENETOCLAX-BASED TIME-LIMITED COMBINATION TREATMENTS (RVE, GVE, GIVE) VS STANDARD CHEMOIMMUNOTHERAPY (CIT: FCR/BR) IN FRONTLINE CHRONIC LYMPHOCYTIC LEUKEMIA OF FIT PATIENTS: FIRST CO-PRIMARY ENDPOINT ANALYSIS OF THE INTERNATIONAL INTERGROUP GAIA (CLL13) TRIAL

Barbara Eichhorst, Carsten U Niemann, Arnon P Kater, Moritz Fürstenau, Julia von Tresckow, Can Zhang, Sandra Robrecht, Michael Gregor, Gunnar Juliusson, Patrick Thornton, Philipp B. Staber, Tamar Tadmor, Vesa Lindström, Caspar da Cunha-Bang, Christoph Schneider, Christian Poulsen, Thomas Illmer, Björn Schöttker, Ann Janssens, Ilse Christiansen, Thomas Nösslinger, Michael Baumann, Marjolein van der Klift, Ulrich Jäger, Henrik Frederiksen, Maria BL Leys, Mels Hoogendoorn, Kourosh Lotfi, Holger Hebart, Tobias Gaska, Harry Koene, Florian Simon,
Nisha De Silva, Anna Fink, Kirsten Fischer, Clemens Wendtner, Karl A Kreuzer, Matthias Ritgen, Monika Brüggemann, Eugen Tausch, Mark-David Levin, Marinus van Oers, Christian Geisler, Stephan Stilgenbauer, Michael Hallek

Coprimary endpoint: uMRD (< 10^{-4}) at Mo15 in PB by 4-colour-flow

ITT analysis: 63 pts (34 CIT, 15 RVe, 10 GVe, 4 GIVe) with missing samples (6.8%) were counted as MRD positive



	uMRD%	97.5% CI
GIVe	92.2	87.3 – 95.7
GVe	86.5	80.6 – 91.1
RVe	57.0	49.5 – 64.2
SCIT	52.0	44.4 – 59.5

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Prof. Dr. med. Peter Borchmann
Uniklinik Köln
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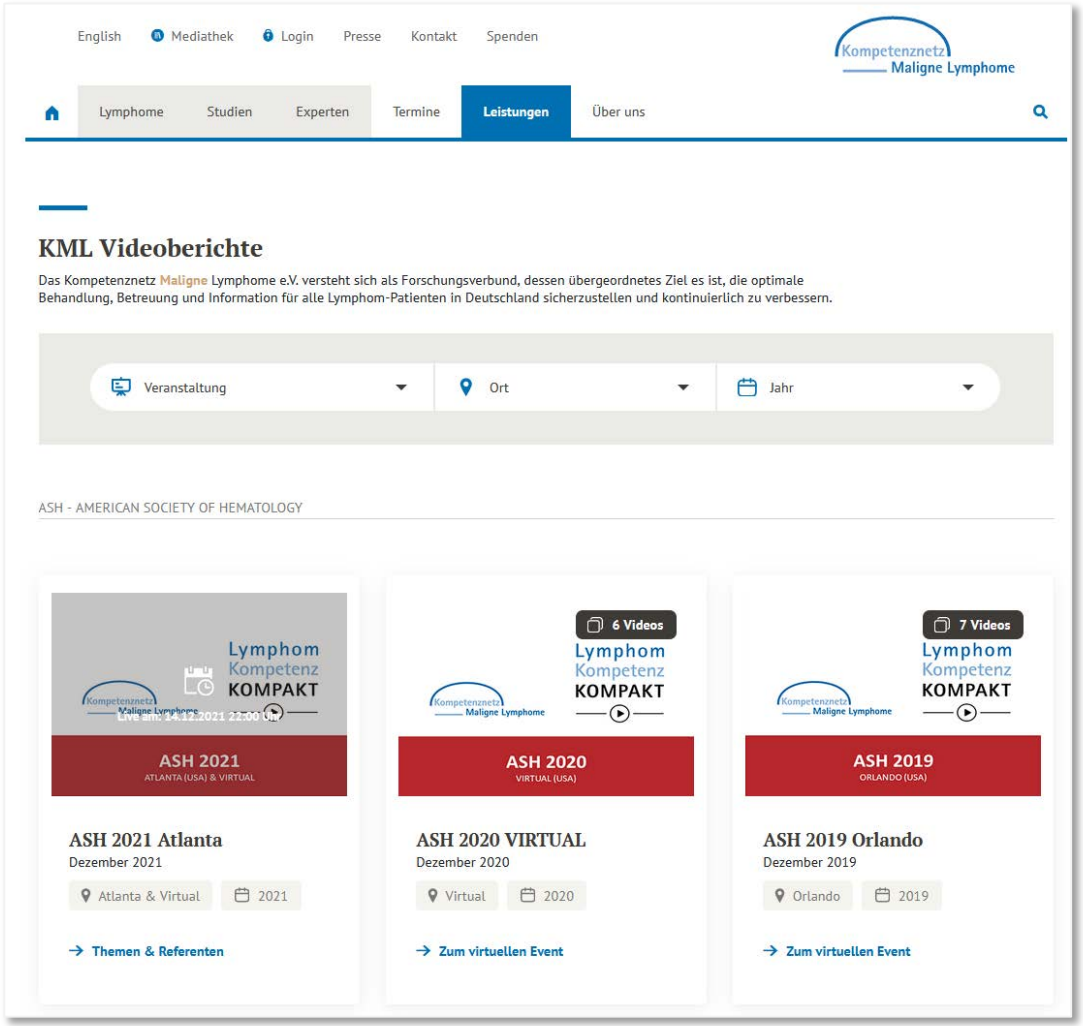
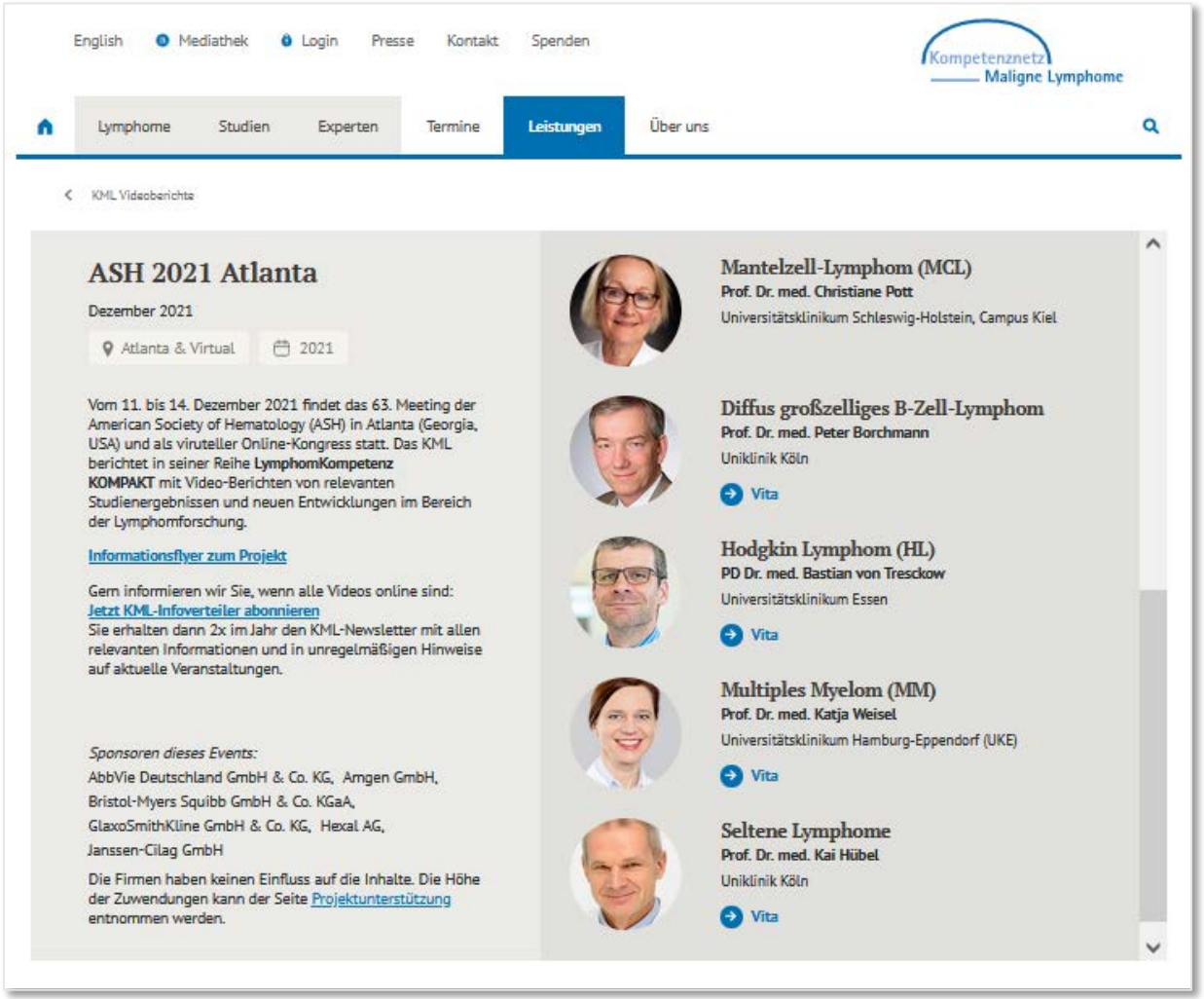
Uniklinik Köln
Seltene Lymphome

Neues Videoportal: www.lymphome.de/kongressberichte





Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2021

Kompetenznetz Maligne Lymphome

Bleiben Sie gut informiert!

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