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Kompetenznetz
Maligne Lymphome

EHA2023 HYBRID

Kompetenznetz Maligne Lymphome

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PD Dr. med. Raphael Koch
Universitätsmedizin Göttingen

T-Zell-Lymphome (T-NHL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – EHA2023 HYBRID wird in Kooperation mit sieben unterstützenden Firmen durchgeführt.
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Anstellungsverhältnis, Führungsposition	Keine
Beratungs-/ Gutachtertätigkeit	Janssen
Besitz von Geschäftsanteilen, Aktien oder Fonds	Keine
Patent, Urheberrecht, Verkaufslizenz	Keine
Honorare	Takeda
Finanzierung wissenschaftlicher Untersuchungen	Inflection Bioscience
Andere finanzielle Beziehungen	Keine
Immaterielle Interessenkonflikte	Keine

Kapitel 1

Stellenwert der 18F-FDG PET/CT in der Primärtherapie

PROGNOSTIC SIGNIFICANCE OF SEQUENTIAL 18F-FDG PET/CT DURING THE TREATMENT OF ANTHRACYCLINE-CONTAINING FRONTLINE CHEMOTHERAPY IN PERIPHERAL T CELL LYMPHOMAS

Abstract P1194

Ga-Young Song[1], Sung-Hoon Jung[1], Seo-Yeon Ahn[1], Mihee Kim[1], Jae-Sook Ahn[1], Je-Jung Lee[1], Hyeoung-Joon Kim[1], Jang Bae Moon[2], Su WoongYoo[2], Seong Young Kwon[2], Jung-Joon Min[2], Hee-Seung Bom[2], Sae-Ryung Kang[2], Deok Hwan Yang*[1]

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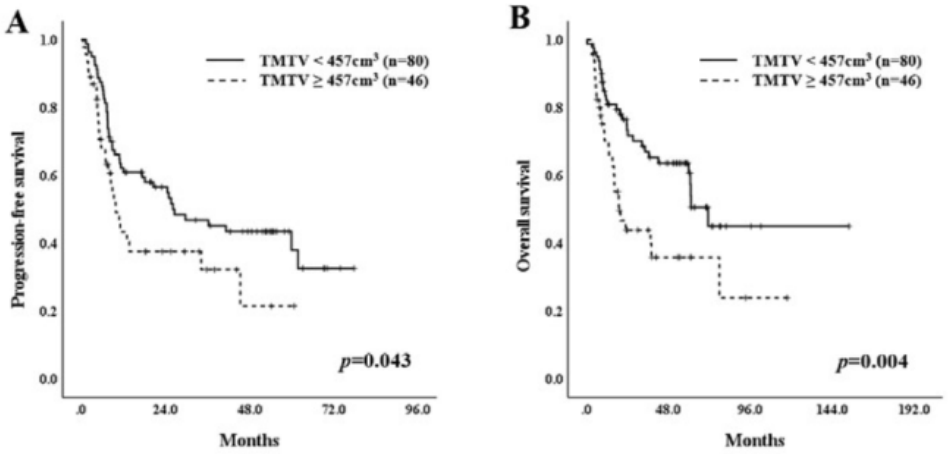
PROGNOSTIC SIGNIFICANCE OF SEQUENTIAL 18F-FDG PET/CT DURING THE TREATMENT OF ANTHRACYCLINE-CONTAINING FRONTLINE CHEMOTHERAPY IN PERIPHERAL T CELL LYMPHOMAS

- Analysis of 143 pts with newly diagnosed PTCL
- All pts treated with anthracyclin-based Chemotherapy
- Sequential 18F-FDG PET/CT at
  - time of diagnosis
  - After 3 cycles of chemotherapy
  - End of chemotherapy
- Baseline total metabolic tumor volume (TMTV) by sum of SUV2.5 method
- Interim PET/CT response by five-point scale (5-PS) of Deauville criteria

- Baseline metabolic tumor volume (MTV) could be calculated in 126 patients. The AUC of TMTV obtained by ROC curve analysis was 0.606 and the cut-off value of TMTV was 457.0cm^3.

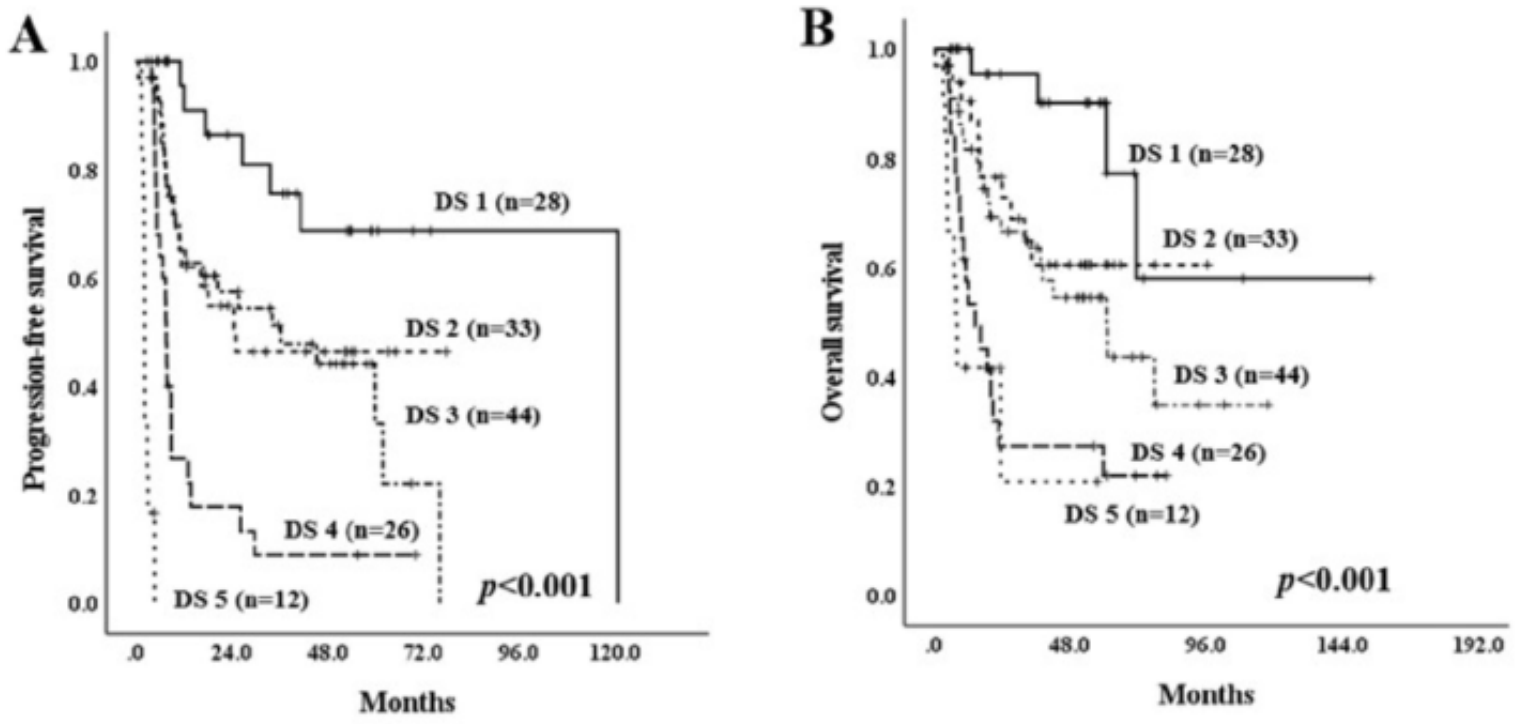


Progression-free survival (PFS) (A) and overall survival (OS) (B) according to baseline total metabolic tumor volume (TMTV)

PROGNOSTIC SIGNIFICANCE OF SEQUENTIAL 18F-FDG PET/CT DURING THE TREATMENT OF ANTHRACYCLINE-CONTAINING FRONTLINE CHEMOTHERAPY IN PERIPHERAL T CELL LYMPHOMAS

Interim PET/CT: n=143

- Score 1: 19.6%
- Score 2: 23.1%
- Score 3: 30.8%
- Score 4: 18.2%
- Score 5: 8.4%



Progression-free survival (PFS) (A) and overall survival (OS) (B) according to interim 18F-FDG PET/CT response assessment using Deauville 5-point scale (PS). PFS (C) and OS (D) according to interim 18F-FDG PET/CT response assessment using Deauville 5-PS when patients were grouped according to DS as DS1, DS2-3, DS4-5

Kapitel 2

Rolle der ALK-Inhibitoren beim ALK+ ALCL nach Therapie mit Brentuximab Vedotin?

Brigatinib in patients with ALK-positive anaplastic large cell lymphoma who have failed brentuximab vedotin

P1166

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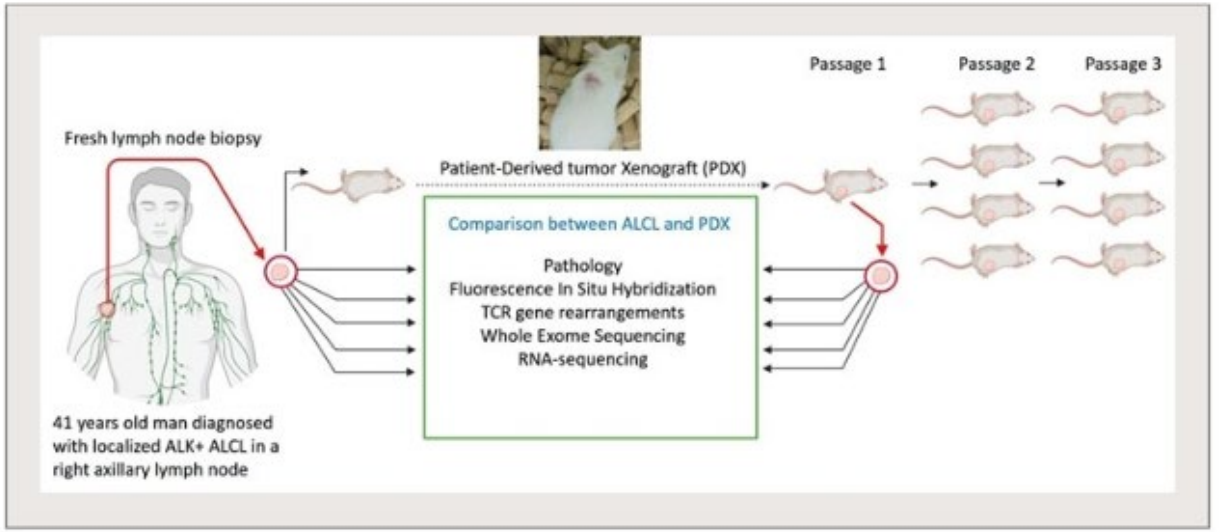
Brigatinib in patients with ALK-positive anaplastic large cell lymphoma who have failed brentuximab vedotin

Welches TKI bei ALK+ ALCL? -> Präklinische Studie

- We generated a patient-derived tumor xenograft (PDX) model from a fresh lymph node biopsy of a newly diagnosed patient with ALK+ ALCL

- We used this PDX model to assess 8 ALK-inhibitors: alectinib, brigatinib, ceritinib, crizotinib, ensartinib, entrectinib, lorlatinib, gilteritinib



Our PDX model closely mimics the patient's primary tumor, both phenotypically and genotypically

Brigatinib in patients with ALK-positive anaplastic large cell lymphoma who have failed brentuximab vedotin

Patients and treatment

- Between Jan 2020 and Oct 2022, 15 French adults who had failed BV started brigatinib
- Pts received brigatinib at a dose of 180 mg once daily (with a 7-day lead-in period at 90 mg), as recommended in ALK-positive NSCLC

n	15
Age (years)	
Median (range)	35 (19-73)
>60	2/15 (13%)
Male	8/15 (53%)
Median time between initial diagnosis and Brigatinib initiation (range, months)	9 (0.5-235)
Median number of prior treatment lines (range)	2 (1-8)
Prior Brentuximab vedotin	15/15 (100%)
In first-line	5/15 (33%)
At relapse/progression	10/15 (67%)
Prior Crizotinib	4/15 (27%)
Primary resistance to crizotinib	2/4
Secondary resistance to crizotinib	1/4
Relapse after discontinuation of crizotinib	1/4
Prior stem cell transplantation	
Autologous	3/15
Allogeneic	1/15
Status at Brigatinib initiation	
Refractory disease	10/15
Relapsed disease	4/15
Not evaluable	1/15
Detectable ALK transcript in blood (RT-PCR)	10/11

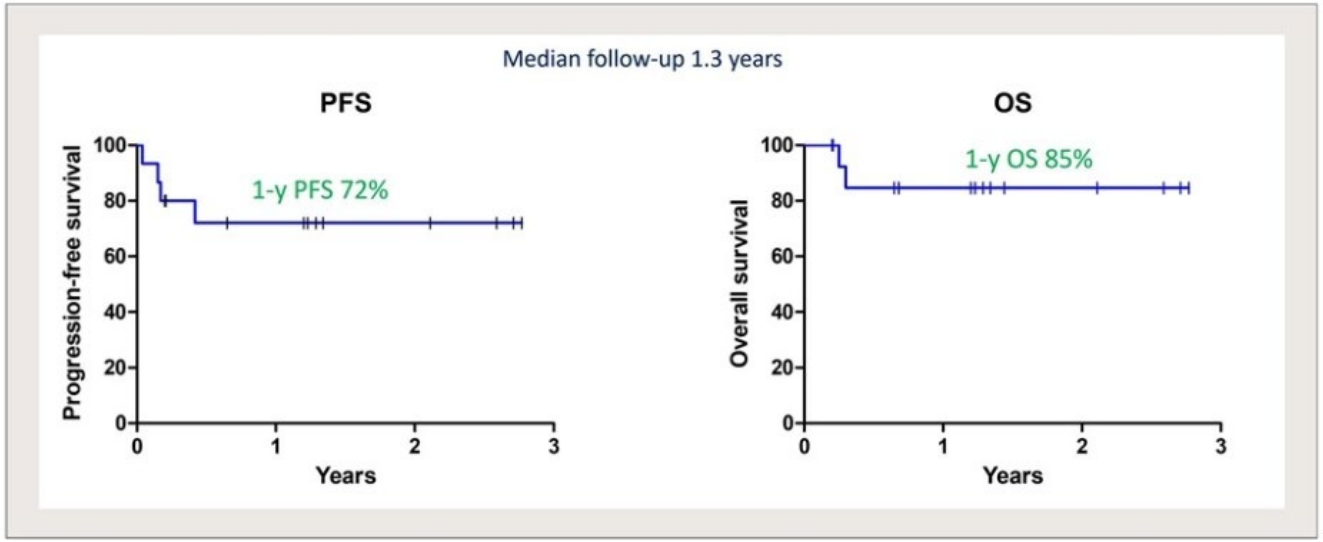
Brigatinib in patients with ALK-positive anaplastic large cell lymphoma who have failed brentuximab vedotin

Efficacy

- The best ORR was 93% (14/15) with 73% (11/15) CR (Lugano response criteria)
  - 2 crizo-R and the crizo-S pts achieved CR, and 1 crizo-R pt reached PR
- 9 pts were monitored for ALK transcript in blood and kinetics correlated with response
- 5 CR pts were bridged to allSCT

Safety and tolerability

- No permanent discontinuation of brigatinib related to adverse event (AE)
- 3 pts had dose reduction for moderate AR (1 dyspnea and 2 cramps), with complete resolution



Kapitel 3

Rezidivtherapie bei AITL, PTCL-NOS, ALCL

DUVELISIB IN PATIENTS WITH RELAPSED/REFRACTORY PERIPHERAL T-CELL LYMPHOMA FROMTHE PHASE 2 PRIMO TRIAL EXPANSION PHASE: OUTCOMES BY BASELINE HISTOLOGY

P1124

Neha Mehta-Shah[1], Eric Jacobsen[*2], Pier Luigi Zinzani[3], Jasmine Zain[4], Monica Mead[5], Carla Casulo[6], Giuseppi Gritti[7], Lauren Pinter-Brown[8], KojiIzutsu[9], Sheila Waters[10], Jonathan Brammer[11], Barbara Pro[12], Steven Horwitz[13]

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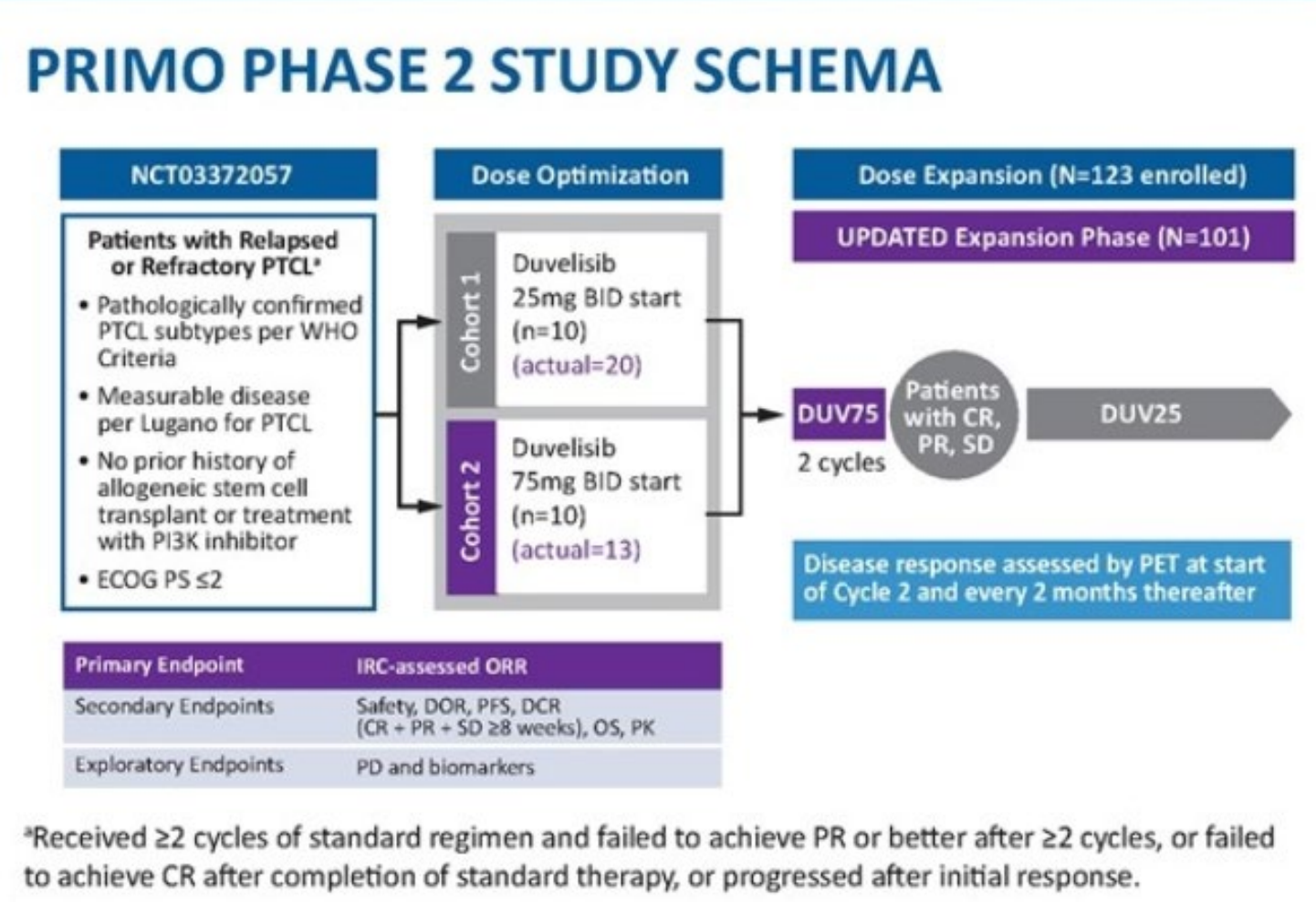
DUVELISIB IN PATIENTS WITH RELAPSED/REFRACTORY PERIPHERAL T-CELL LYMPHOMA FROMTHE PHASE 2 PRIMO TRIAL EXPANSION PHASE: OUTCOMES BY BASELINE HISTOLOGY



[a]Received ≥2 cycles of standard regimen and failed to achieve PR or better after ≥2 cycles, or failed to achieve CR after completion of standard therapy, or progressed after initial response.

DUVELISIB IN PATIENTS WITH RELAPSED/REFRACTORY PERIPHERAL T-CELL LYMPHOMA FROMTHE PHASE 2 PRIMO TRIAL EXPANSION PHASE: OUTCOMES BY BASELINE HISTOLOGY

BASELINE CHARACTERISTICS

- The updated analysis of the PRIMO-EP included 101 patients

Characteristic	PRIMO-EP (N=101)
Median age (range), years	67.0 (21 – 92)
≥65 years, n (%)	55 (54.5)
Male, n (%)	54 (53.5)
Race, (n) %	
White	73 (72.3)
Asian	18 (17.8)
Black or African American	6 (5.9)
Other	4 (4.0)
Median time from initial diagnosis (range), months	19.7 (0 – 196)
Median time from most recent R/R diagnosis (range), months	1.2 (0 – 143)
Baseline histology, n (%)	
PTCL-NOS	52 (51.5)
AITL	30 (29.7)
ALCL	15 (14.9)
Other*	4 (4.0)
Median number of prior anticancer therapies (range)	3 (1 – 9)
Type of prior anticancer therapy	
CHOEP/EPOCH	37 (36.6)
CHOP/RCHOP	37 (36.6)
BV/BV-containing chemotherapy	37 (36.6)
Salvage chemo after CHOP/RCHOP or CHOEP/EPOCH	38 (37.6)
Autologous stem cell transplant	22 (21.8)

*1 each, EATL, EBV associated lymphoma, DLBCL, and TCL; 1 DLBCL was not in alignment with inclusion criteria.

ADVERSE EVENTS (ALL CAUSALITY) IN >5% OF PATIENTS WITH MAXIMUM GRADE 3 AND MAXIMUM GRADE 4

Adverse Event (All Causality) in >5% of Patients	PRIMO-EP (N=101), n (%)[7]
AE ≤ Grade 3	
Alanine aminotransferase increased	15 (14.9)
Aspartate aminotransferase increased	14 (13.9)
Diarrhea	8 (7.9)
Neutropenia/neutrophil count decreased	14 (13.9)
Rash maculopapular	8 (7.9)
AE ≤ Grade 4	
Alanine aminotransferase increased	6 (5.9)

Note: If a subject experienced multiple incidents of events for a given system organ class or preferred term, the subject was counted only once for the event with maximum grade per system organ class or preferred term, accordingly. Events are counted at each grade observed.

DUVELISIB IN PATIENTS WITH RELAPSED/REFRACTORY PERIPHERAL T-CELL LYMPHOMA FROMTHE PHASE 2 PRIMO TRIAL EXPANSION PHASE: OUTCOMES BY BASELINE HISTOLOGY

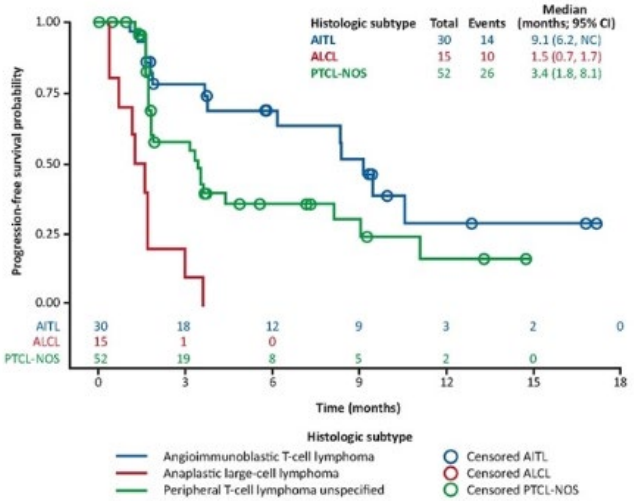
EFFICACY OUTCOMES – PRIMO EP

- The ORR by IRC was 49% with a CR rate of 34%; responses were seen across multiple subtypes

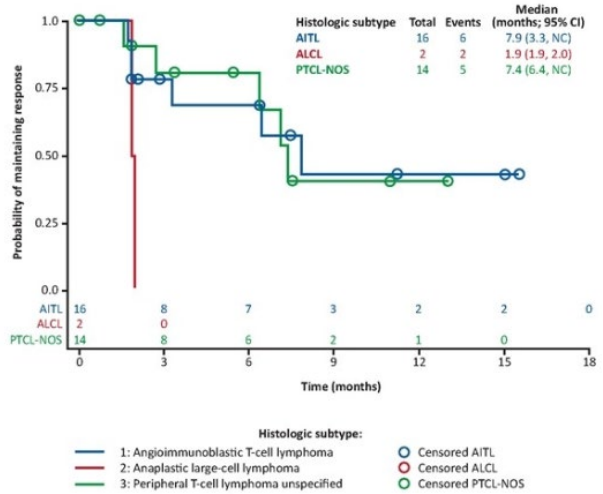
Outcome	PRIMO-EP (N=101)*
ORR by IRC, n (%) [95% CI]	49 (48.5) [38.8 – 58.3]
ORR by PTCL subtype by IRC, n (% of histology subgroup)	
PTCL-NOS	25/52 (48.1)
AITL	20/30 (66.7)
ALCL	2/15 (13.3)
Other[a]	2/4 (50.0)
Best overall response, n (%)	
Complete response (CR)	34 (33.7)
CR by PTCL subtype, n (% of histology subgroup)	
PTCL-NOS	14/52 (26.9)
AITL	16/30 (53.3)
ALCL	2/15 (13.3)
Other[a]	2/4 (50.0)
Partial response (PR)	15 (14.9)
Stable disease (SD)	2 (2.0)

*Modified intent-to-treat analysis set = any patient who received at least 1 dose of duvelisib;
[a]1 T-cell Lymphoma, 1 DLBCL was not in alignment with inclusion criteria.

PFS BY HISTOLOGY



DURATION OF COMPLETE RESPONSE BY HISTOLOGY



Conclusions

- Response to duvelisib was seen in 49% of patients, with 34% achieving a complete response
- Response by histology were higher in patients with AITL (66.7%) and PTCL-NOS (48.1%) compared with ALCL (13.3%)

Kapitel 4

Die Rolle der allogenen Stammzelltransplantation beim NK/T-Zell Lymphom

ALLOGENEIC STEM CELL TRANSPLANTATION FOR NK/T-CELL LYMPHOMA IN THE ERA OFASPARAGINASE-BASED CHEMOTHERAPY: A RETROSPECTIVE ANALYSIS OF THE EBMT LYMPHOMA WORKING PARTY

S225

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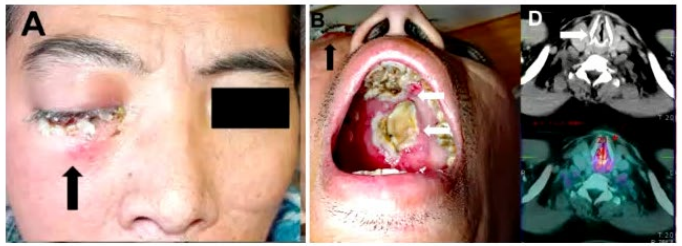
ALLOGENEIC STEM CELL TRANSPLANTATION FOR NK/T-CELL LYMPHOMA IN THE ERA OFASPARAGINASE-BASED CHEMOTHERAPY: A RETROSPECTIVE ANALYSIS OF THE EBMT LYMPHOMA WORKING PARTY

Introduction

Major characteristics of Natural Killer/T-cell lymphomas

- rare and aggressive lymphoma of NK/T-cell origin
- related to EBV infection affecting *p53*
- comprises 5-10% of all NHL in Asia and South America, rare in Europe and US
- median age at diagnosis about 50 years, male predominance (2:1)



Tse et al., J Hematol Oncol 2022

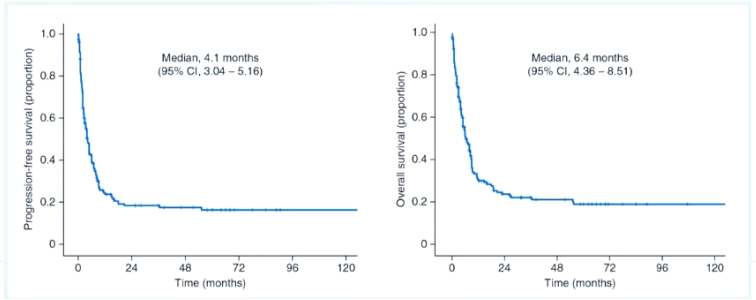
Treatment remains challenging

Asparaginase-containing regimens represent standard first-line therapy

- Approx. 50% of patients with advanced stage achieve long-term survival
- Anthracycline-based regimens have been largely abandoned (multi-drug resistance!)

Very poor prognosis in relapsed / refractory ENKTCL

- PFS and OS after first relapse / progression treated with non-anthracycline-based chemotherapy



Lim et al., *Annals of Oncology* 2017

ALLOGENEIC STEM CELL TRANSPLANTATION FOR NK/T-CELL LYMPHOMA IN THE ERA OFASPARAGINASE-BASED CHEMOTHERAPY: A RETROSPECTIVE ANALYSIS OF THE EBMT LYMPHOMA WORKING PARTY

Methods

Retrospective analysis of EBMT registry and data from Chinese and Korean centers

Patient characteristics

Variable	N = 135 (%)
Age at transplantation, median (range)	43.4 (18.3-67.7)
Male Sex	92 (68.1)
Region	
Europe (EBMT)	97 (71.9)
Asia	38 (28.1)
Disease stage at diagnosis	
Localized (I-II)	40 (30.0)
Advanced (III-IV)	83 (61.4)
Unknown	12 (8.6)
PINK score	
Low	14 (10.4)
Intermediate	15 (11.1)
High	60 (44.4)
Unknown	46 (34.1)

Variable	N = 135 (%)
First-line therapy	
Anthracycline-based	36 (26.7)
L-Asparaginase-based	68 (50.4)
DeVIC or VIPD	8 (5.9)
Gemcitabine-based	1 (0.7)
Other	14 (10.4)
Unknown	8 (5.9)
Radiotherapy in first-line	44 (32.6)
Prior autologous transplantation	28 (20.7)
Number of prior therapies	
1	27 (20.0)
2	45 (33.3)
3 or more	58 (43.0)
Unknown	5 (3.7)

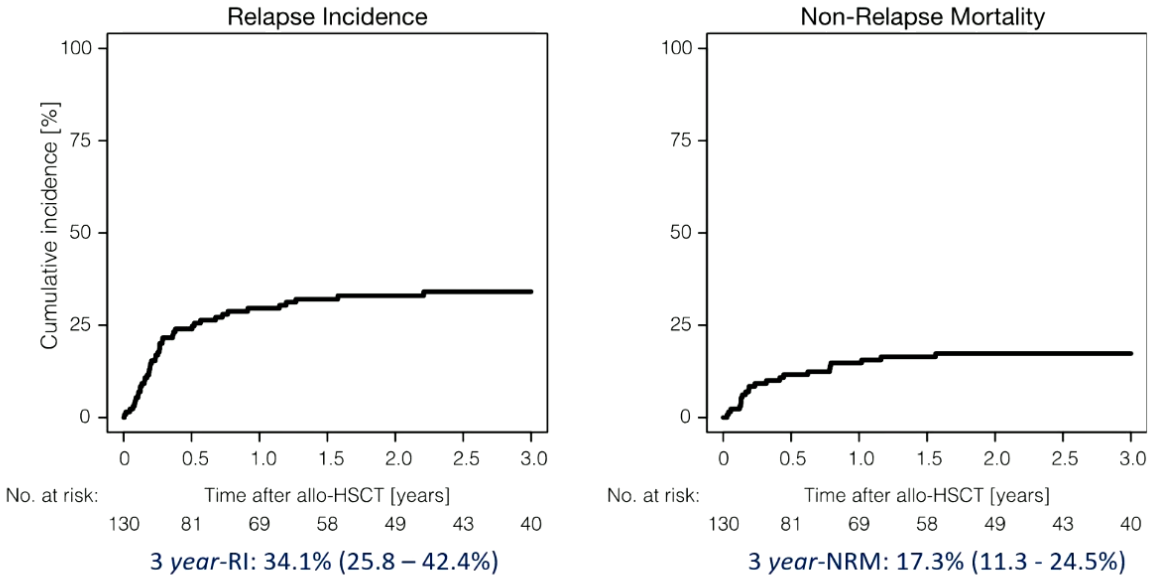
Patient characteristics at Transplantation

Variable	N = 135 (%)
Asparaginase-containing therapy (before HSCT)	100 (74.1)
Status at transplantation	
CR	71 (52.6)
PR	36 (26.7)
SD	3 (2.2)
PD	24 (17.8)
Donor Type	
Matched related	48 (35.6)
Unrelated	59 (43.7)
Haploidentical	27 (20.0)
Stem cell source	
Bone marrow	12 (8.9)
Peripheral blood	123 (91.1)

Variable	N = 135 (%)
Conditioning regimen	
RIC	63 (46.7)
MAC	72 (53.3)
TBI in the conditioning regimen	35 (25.9)
GVHD prophylaxis	
Cyclosporin A alone	14 (10.4)
Cyclosporin A + MTX	33 (24.4)
Cyclosporin A + MMF	18 (13.3)
Cyclosporin A + MMF + MTX	27 (20.0)
Tacrolimus + MTX	6 (4.5)
Tacrolimus + MMF	6 (4.5)
Other	30 (22.2)

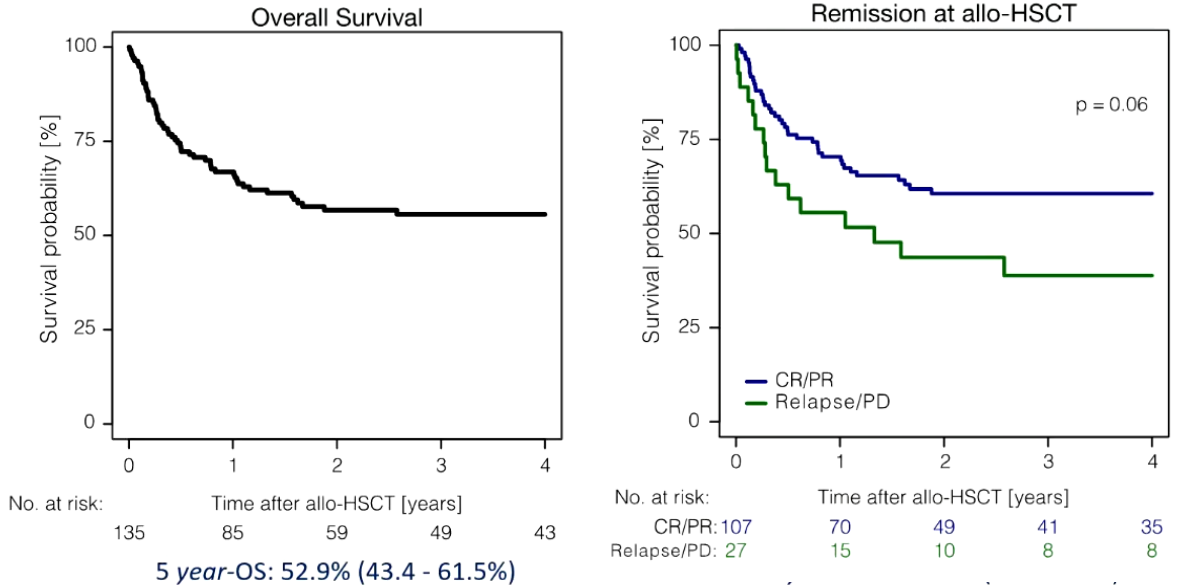
ALLOGENEIC STEM CELL TRANSPLANTATION FOR NK/T-CELL LYMPHOMA IN THE ERA OFASPARAGINASE-BASED CHEMOTHERAPY: A RETROSPECTIVE ANALYSIS OF THE EBMT LYMPHOMA WORKING PARTY

Relapse Incidence and Non-Relapse Mortality



Median follow-up: 4.8 years (95% CI: 3.7 - 5.9)

Survival after allo-HSCT



Median follow-up: 4.8 years (95% CI: 3.7 - 5.9)

Zusammenfassung | Take-Home-Messages

- Die Rolle des 18F-FDG PET/CT zur Prognoseeinschätzung bei PTCLs i.R. der Primärtherapie wird weiter gestützt.
- Im ALK+ ALCL zeigt Brigatinib bei Patienten im Rezidiv/Progress nach Brentuximab Vedotin in einer Fallserie vielversprechende Effektivität und gute Verträglichkeit.
- Der PI3K-Inhibitor Duvelisib zeigt Subtyp-abhängige klinische Aktivität, v.a. im AITL und PTCL-NOS.
- Rezidiviertes / refraktäres NK/T-Zell Lymphom: Langzeitüberleben durch allogene Stammzelltransplantation erreichbar.

Die Kurzpräsentationen sind online unter

www.lymphome.de/eha2023

Für den Inhalt verantwortlich:

PD Dr. med. Raphael Koch

Universitätsmedizin Göttingen

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

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