Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

15-ICML

15th International Conference on Malignant Lymphoma
Palazzo dei Congressi, Lugano, Switzerland, June 18-22, 2019

18.–22. Juni 2019

KML-Experten berichten vom 15-ICML 2019 in Lugano

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT 15-ICML 18.–22. Juni 2019

Prof. Dr. med. Gerald Illerhaus

ZNS Lymphome

Ärztlicher Direktor der Klinik für Hämatologie, Onkologie und Palliativmedizin am Klinikum Stuttgart|
Leiter Kooperative Studiengruppe ZNS-Lymphome

Interessenskonflikte

1. **Employment or Leadership Position**
   Klinikum Stuttgart
2. **Advisory Role**
   Riemser, Celgene
3. **Stock Ownership**
   none
4. **Honoraria**
   Riemser, Celgene
5. **Financing of Scientific Research**
   Riemser
6. **Expert Testimony**
   Celgene, Riemser
7. **Other Financial Relationships**
   none

15. ICML - Inhalt

1. **Erstlinientherapie ältere Patienten mit PCNSL**
2. **Rezidivtherapie bei PCNSL**
3. **SCNSL-Register**
4. **Intraokuläre Lymphome**

Hochdosischemotherapie bei älteren Patienten mit Primären ZNS-Lymphomen

- Können ältere Patienten mit einer kurzen, dosisintensivierten Therapie mit abschließender altersangepasster Hochdosischemotherapie sicher und effektiv behandelt werden?

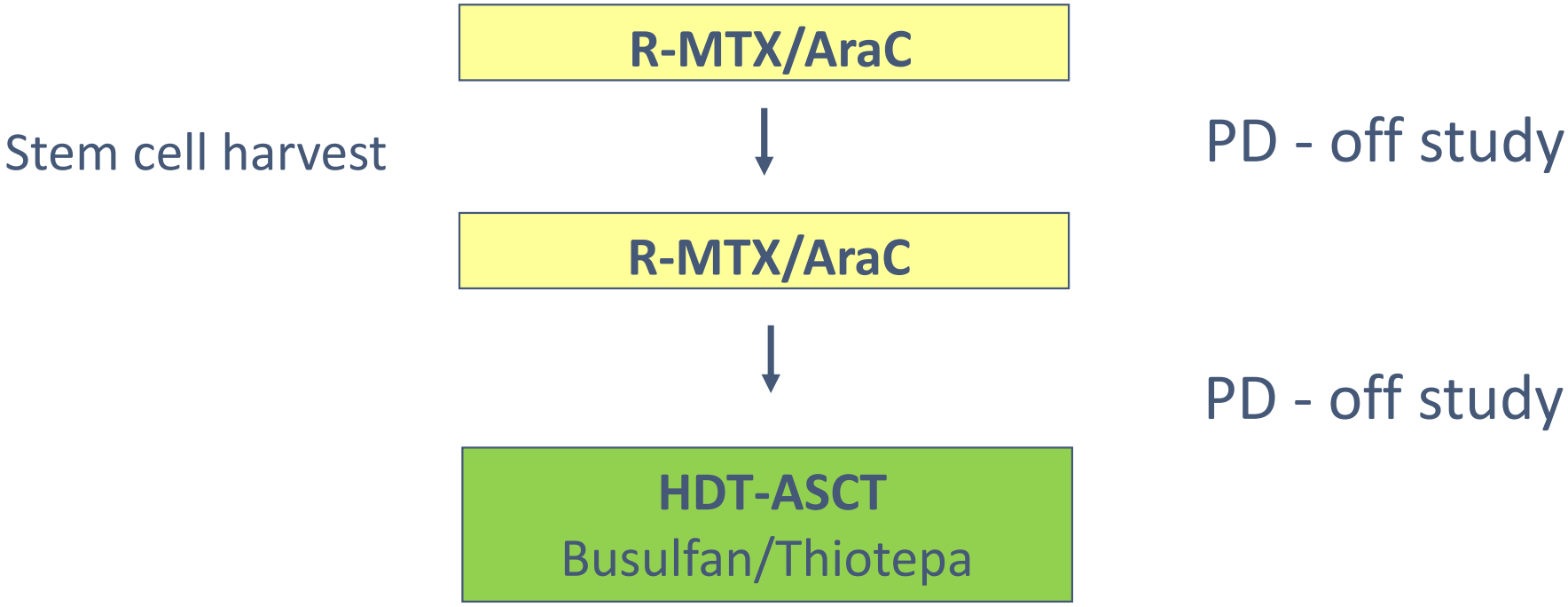
Abstract 217

Bicentric pilot study on age-adapted high-dose chemotherapy and autologous stem cell transplant in newly diagnosed primary CNS lymphoma patients > 65 years - MARiTA Trial

E. Schorb[1], B. Kasenda[2,3], G. Ihorst[1,4], H. Fricker[1], H-G. Holl[2], J. Finke[1], G. Illerhaus[2]

[1] Department of Hematology and Oncology, Medical Center, Faculty of Medicine, University of Freiburg; Germany; [2] Department of Hematology, Oncology and Palliative Care, Klinikum Stuttgart, Stuttgart, Germany; [3] Department of Medical Oncology, University Hospital Basel, Basel, Switzerland, [4] Clinical Trials Unit, Medical Center, Faculty of Medicine, University of Freiburg; Germany.

Studiendesign



MARITA-Trial

Trial design

Prospective, single-arm, pilot study conducted at two German centers between December 2015 and September 2017.

Main eligibility criteria:

- newly diagnosed PCNSL
- Immunocompetency
- age > 65 years
- ECOG PS ≤ 2
- adequate organ function.

Main endpoints:

- toxicity,
- lymphoma response
- progression free survival (PFS)
- overall survival (OS).

MARITA-Trial

Patient characteristics (n=14)	
Age (median, range)	73 (69-79)
Sex (female) (%)	8/14 (57%)
KPS (%,median, range)	80 (30-90)
CIRS Score (median, range)	4 (4-6)
Involvement of deep brain structures	4/14 (29%)
Serum-LDH erhöht (%)	6/13 (46%)
CSF involvement (%)	2/12 (17%)
Ocular involvement (%)	0/11 (0%)
Histology: DLBCL	14/14 (100%)
Therapy line: first-line	14/14 (100%)
Collected stem cells (median)	9,99 Mio/kgKG

Feasibility and Response

Rituximab 375mg/m² (d 0,-4)
Methotrexate 3,5 g/m² i.v. (d1)
Cytarabine 2x2 g/m²/d i.v. (d2-3)

SC Harvest

Rituximab 375mg/m² (d 0,-4)
Methotrexate 3,5 g/m² i.v. (d1)
Cytarabine 2x2 g/m²/d i.v. (d2-3)

MRI Response Assessment

Busulfan 3,2 mg/kg/d i.v. (d-7-(-6))
Thiotepa 5 mg/kg/d i.v. (d-5-(-4))
ASZT (d0)

14 Patients (ITT)

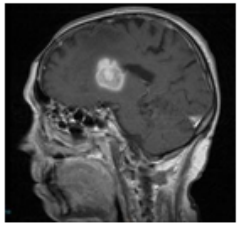
1 off study
(hypervolaemia, preexisting cardiac comorbiditiy)

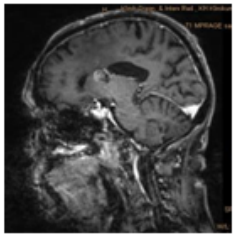
13 Patients (93%)

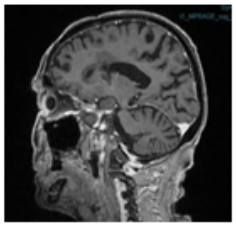
2 CR, 11 PR

13 Patients (93%)

12 CR, 1 PR







Main Toxicity

Toxicity (grade 3/4)	1st cycle (n=14)	2nd cycle (n=13)	HCT-ASCT (n=13)
thrombocytopenia	14 (100%)	11 (85%)	13 (100%)
anemia	3 (21%)	13 (100%)	13 (100%)
neutropenia	5 (36%)	6 (17%)	8 (62%)
febrile neutropenia	**2 (14%)**	**4 (31%)**	**11 (85%)**
infections	**3 (21%)**	**5 (38%)**	**4 (31%)**
elevated transaminases	10 (71%)	1 (8%)	1 (8%)
mucositis	0 (0%)	0 (0%)	5 (38%)
hyperglycemia	1 (7%)	2 (15%)	2 (15%)
hypertension	2(14%)	0 (0%)	1 (8%)
fever	0 (0%)	1 (8%)	1 (8%)
fatigue	0 (0%)	1 (8%)	1 (8%)
hemorrhoidal bleeding	1 (7%)	1 (8%)	0 (0%)
atrial fibrillation	1 (7%)	0 (0%)	0 (0%)
anorexia	0 (0%)	1 (8%)	0 (0%)
nausea	0 (0%)	1 (8%)	0 (0%)
confusion	0 (0%)	0 (0%)	1 (8%)
syncope	0 (0%)	0 (0%)	1 (8%)
hypotension	1 (7%)	0 (0%)	0 (0%)

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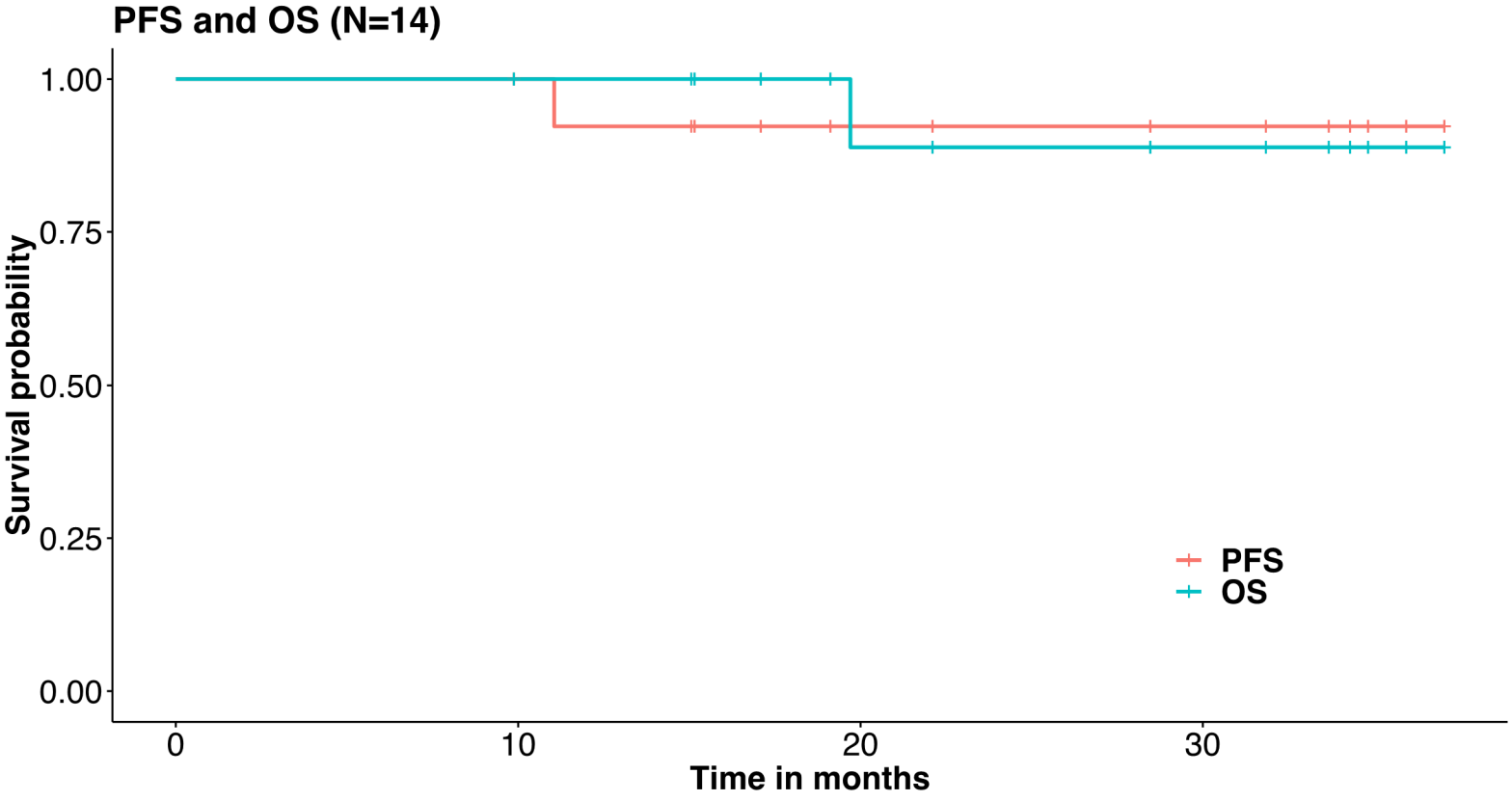
no treatment related mortality

Survival (median Follow-up: 29 mo)



Neues zur Rezidivtherapie bei Primären ZNS-Lymphomen

- Wirkt R-CHOP unter Hinzugabe eines die Bluthirnschranke öffnenden Agens bei ZNS-Lymphomen?
- Ermöglicht der modifizierte Tumor Necrosis Factor den Durchtritt der „klassischen Zytostatika“ ins ZNS

Abstract 109

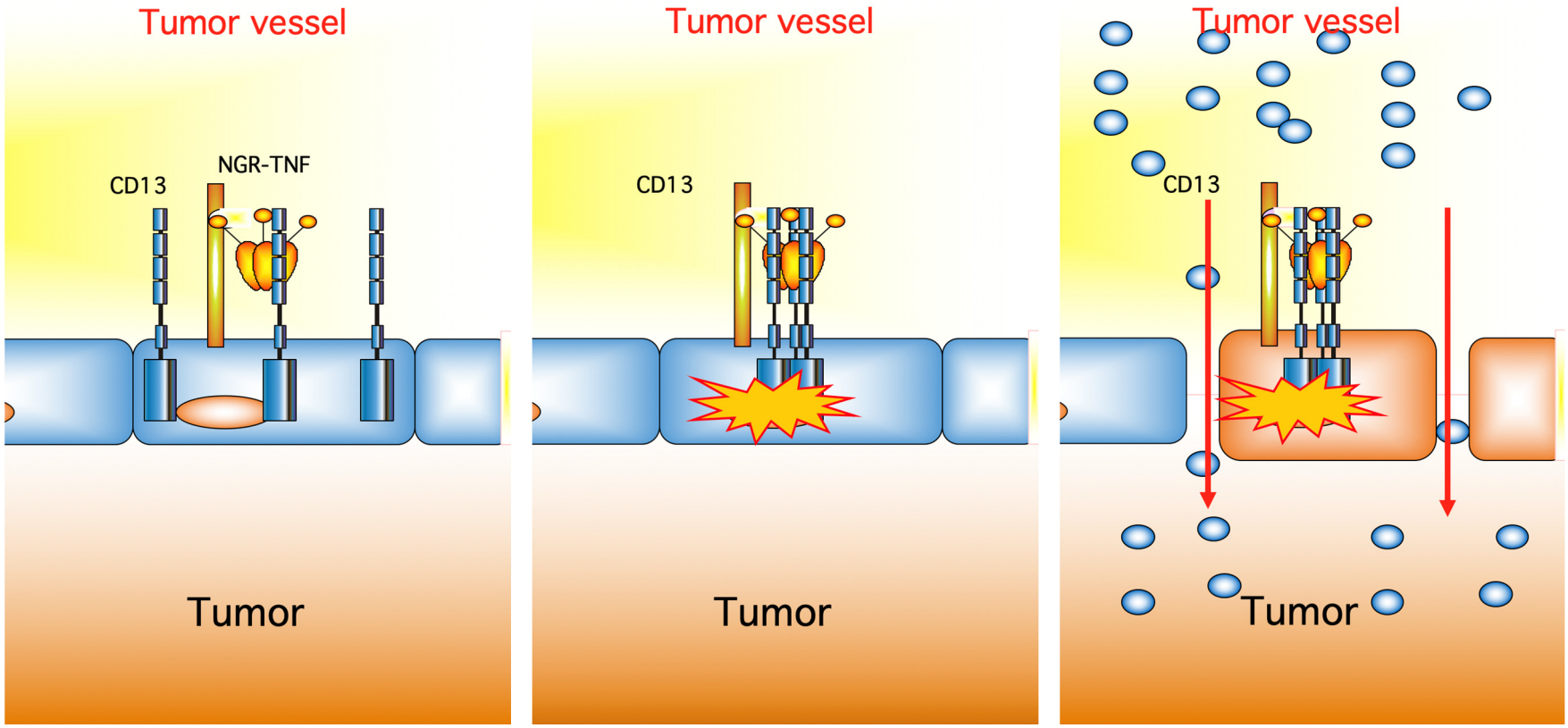
R-CHOP Preceded by Engineered Tumor Necrosis Factor in Relapsed or Refractory Primary DLBCL of the CNS: Final Results of the "INGRID" Trial

A.J.M. Ferreri, T. Calimeri, G. Marco Conte, M. Ponzoni, Federico F., D. Cattaneo[1], E. Scarano, F. Curnis, M. Sassone, M. Foppoli, S. Perrone, C. Cecchetti, P. Lopedote, F. Ciceri, C. Bordignon[2], N. Anzalone, A. Corti

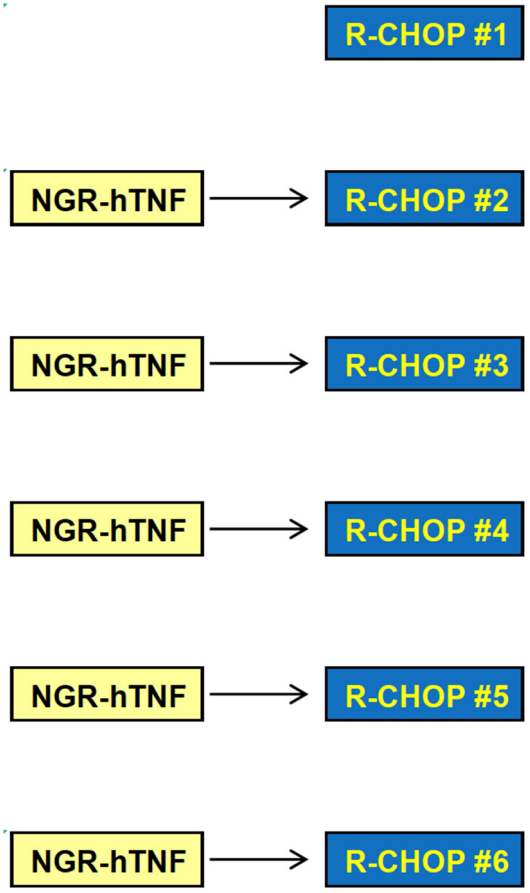
IRCCS San Raffaele Scientific Institute, Milano, Italy;
[1]ASST Fatebenefratelli Sacco University Hospital, Milano, Italy
[2]Molmed srl, Milano, Italy

INGRID-Trial

Hintergrund:



INGRID-Trial - Studiendesign



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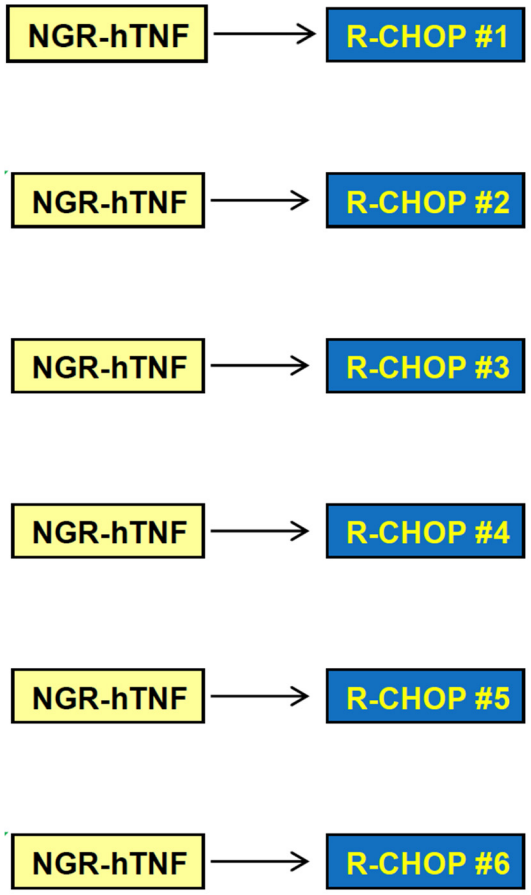


INGRID-Trial

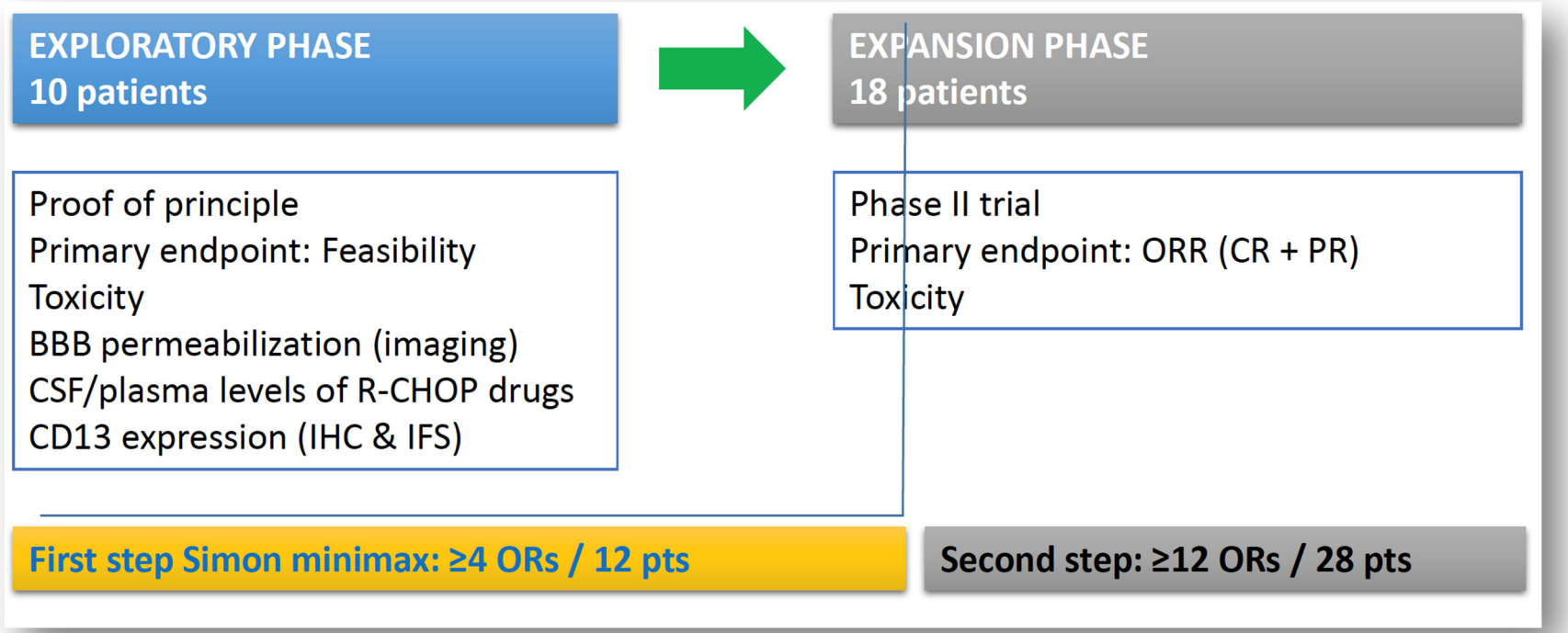
Untersuchungen:

- **DCE MRI:**
  Variations in the BBB of the tumor and perilesional areas.
- **SPECT:**
  99mTc-DTPA penetrate the disrupted BBB
- **Specificity of BBBp:**
  Concentrations of rituximab, CTX and DOXO in matched CSF and plasma samples.

BBBp: blood-brain barrier permeabilization; **DCE-MRI:** dynamic contrast-enhanced MRI
SPECT: 99mTc-DTPA single photon emission computed tomography.

INGRID-Trial

Durchführung:



INGRID-Trial

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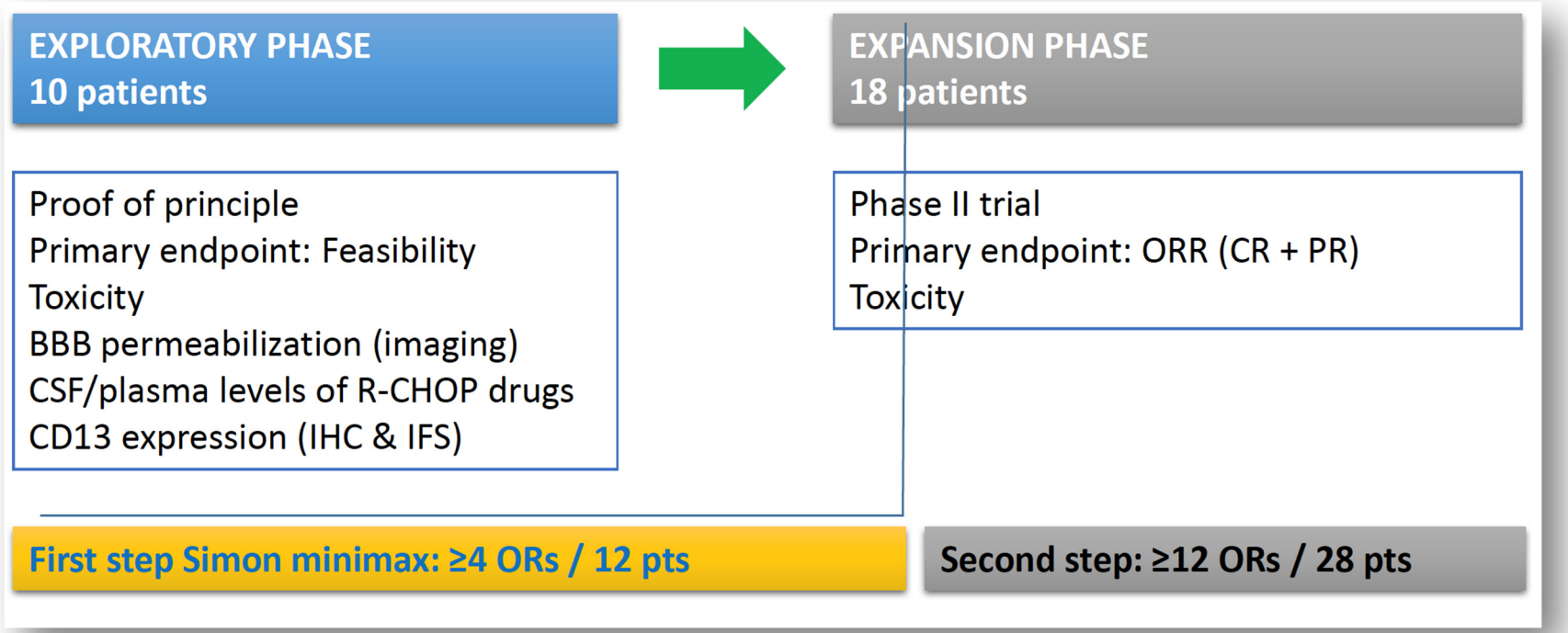


28 Patients

- Progressive or recurrent disease
- Previous treatment with HD-MTX-based chemo ±WBRT

INGRID-Trial

Feasibility:

- Experimental treatment was well tolerated.
- 134 (80%) of the 168 planned courses were delivered
- 19 pts received the 6 planned courses; interruptions in 9 pts due to PD.
- No cases of unexpected toxicity and no required dose reductions.

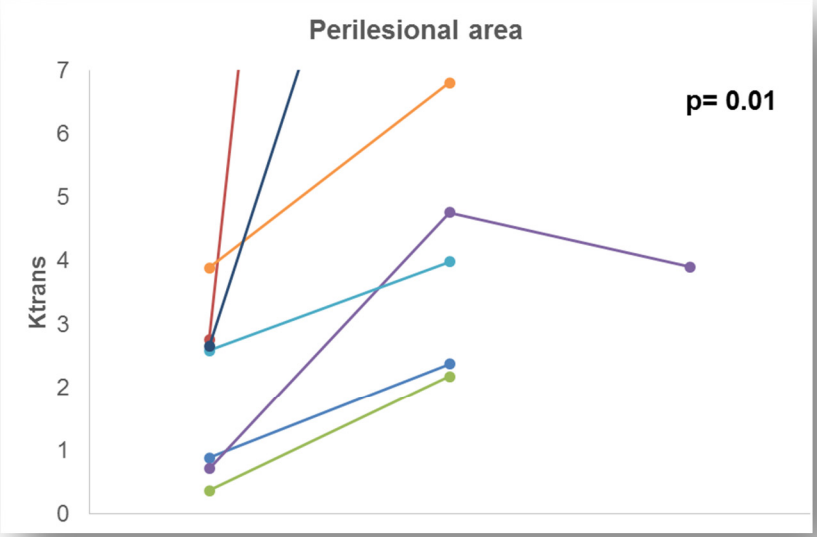
Toxicity:

Grade	1 – 2	3	4	5
Neutropenia	10 (8%)	17 (13%)	58 (44%)	-
Thrombocytopenia	32 (24%)	24 (18%)	26 (20%)	-
Anaemia	86 (66%)	12 (10%)	2 (2%)	-
Febrile Neutropenia	-	5 (4%)	1 (1%)*	-
Hepatotoxicity	25 (19%)	4 (3%)	1 (1%)	-
Oral Mucositis	-	3 (2%)	-	-
Infections	-	5 (4%)*	-	-
Seizures	3 (2%)*	-	-	-
Deep Vein Thrombosis	2 (2%)*	-	-	-
Syncope		2 (2%)*		
LVEF reduction	1 (1%)*	-	-	-
Constipation	2 (2%)	1 (1%)*	-	-
Probable IPA	-	1 (1%)*	-	-
TNF Infusion reaction	7 (5%)	-	-	-

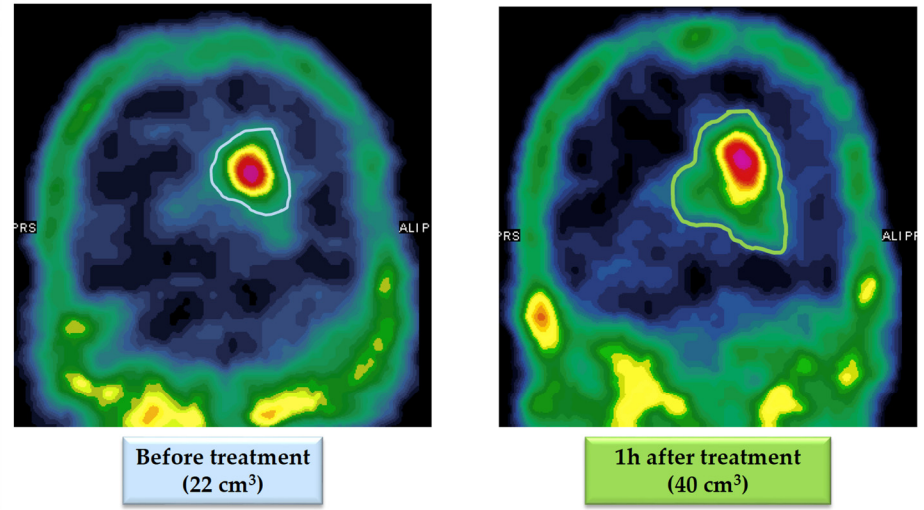
INGRID-Trial

BBB permeability :

DCE-MRI:



SPECT:



INGRID-Trial

Response:

Overall Response	21	(75%)	95% CI: 64-86%
CR	12	(43%)	95% CI: 24-60%
PR	9	(32%)	
PD	7	(25%)	

INGRID-Trial

Response:

Overall Response	21	(75%)	95% CI: 64-86%
CR	12	(43%)	95% CI: 24-60%
PR	9	(32%)	
PD	7	(25%)	

Consolidation	(n= 21)
WBRT	7
ASCT	5
Lenalidomide	1
Multiple	4
Total	17

INGRID-Trial

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Consolidation	(n= 21)
WBRT	7
ASCT	5
Lenalidomide	1
Multiple	4
Total	17

median follow-up: 12 (4-20) months:

→ 8 pts remain relapse free, 9 pts are alive.

Register für sekundäre ZNS-Lymphome

- Prospektive Analyse mit 181 Patienten

Abstract 200

Prospective multicenter registry for secondary CNS involvement in malignant lymphoma: an update with data from 181 patients

F. Lammer [1], L. May [1], P. Martus [2], R. Schroers [3], U. Schlegel [4], S. Hofer [5], O. Bairey [6], N. Schmitz [7], F. Griesinger [8], M. Schmidt-Hieber [9], F. Weißinger [10], P. Reimer [11], P. le Coutre [1], P. Fix [12], O. Hopfer [13], C. Junghanß [14], H. Höffkes [15], B. Heilmeier [16], R. Möhle [17], E. Lange [18], A. Korfel[1]*, U. Keller [1]*

1 Haematology, Oncology, Charité University Medicine, Berlin, Germany, 2 Institute of Clinical Epidemiology and Applied Biostatistics, University Hospital Tübingen,, Tübingen, Germany, 3 Haematology, Oncology, Knappschaftskrankenhaus, Ruhr-Universität Bochum, Bochum, Germany, 4 Neurology, Knappschaftskrankenhaus, Ruhr-Universität Bochum, Bochum, Germany, 5 Oncology, Luzerner Kantonsspital, Luzern, Switzerland, 6 Haematology, Tel Aviv University, Tel Aviv, Israel, 7 Haematology, Oncology, Universitätsklinikum Münster, Münster, Germany, 8 Haematology, Oncology, Pius Hospital Oldenburg, Oldenburg, Germany, 9 Haematology, Oncology, Carl-Thiem-Klinikum, Cottbus, Germany, 10 Haematology, Oncology, Evangelisches Klinikum Bethel, Bielefeld, Germany, 11 Haematology, Oncology, St. Josef Krankenhaus Essen Werden, Essen, Germany, 12 Haematology, Oncology, Klinikum Weimar, Weimar, Germany, 13 Haematology, Oncology, Klinikum Frankfurt (Oder), Frankfurt (Oder), Germany, 14 Haematology, Oncology, University Rostock, Rostock, Germany, 15 Haematology, Oncology, Klinikum Fulda, Fulda, Germany, 16 Oncology, Krankenhaus Barmherzige Brüder, Regensburg,Germany, 17 Haematology, Oncology, University Hospital Tübingen, Tübingen, Germany, 18 Haematology, Oncology, Evangelisches Krankenhaus Hamm, Hamm, Germany.

Background

- Secondary central nervous system (CNS) involvement is a rare (<5%) complication of systemic lymphoma
- Poor prognosis → median OS < 6 months
- Optimal management for SCNSL is yet to be defined

SCNSL-Register

Background

- Secondary central nervous system (CNS) involvement is a rare (<5%) complication of systemic lymphoma
- Poor prognosis → median OS < 6 months
- Optimal management for SCNSL is yet to be defined

Methods

- Since July 2011, 237 patients were included.
- Data of the first 181 patients are presented

Results

- Median age: 63 years
- CNS-mainfestation at initial diagnosis: 31 (17%)
- CNS disease at relapse: 150 (83%)

- Histology:

  - aggressive B-/T-cell NHL: 151 (84%)

  - indolent NHL: 29 (16%)

Treatment (n=177)

- Combined systemic and intrathecal: 83 (47%)
- Systemic therapy alone 72 (41%)
- other 22 (12%)

- HD-MTX (79%)
- HD-AraC (56%)
- Rituximab (63%)

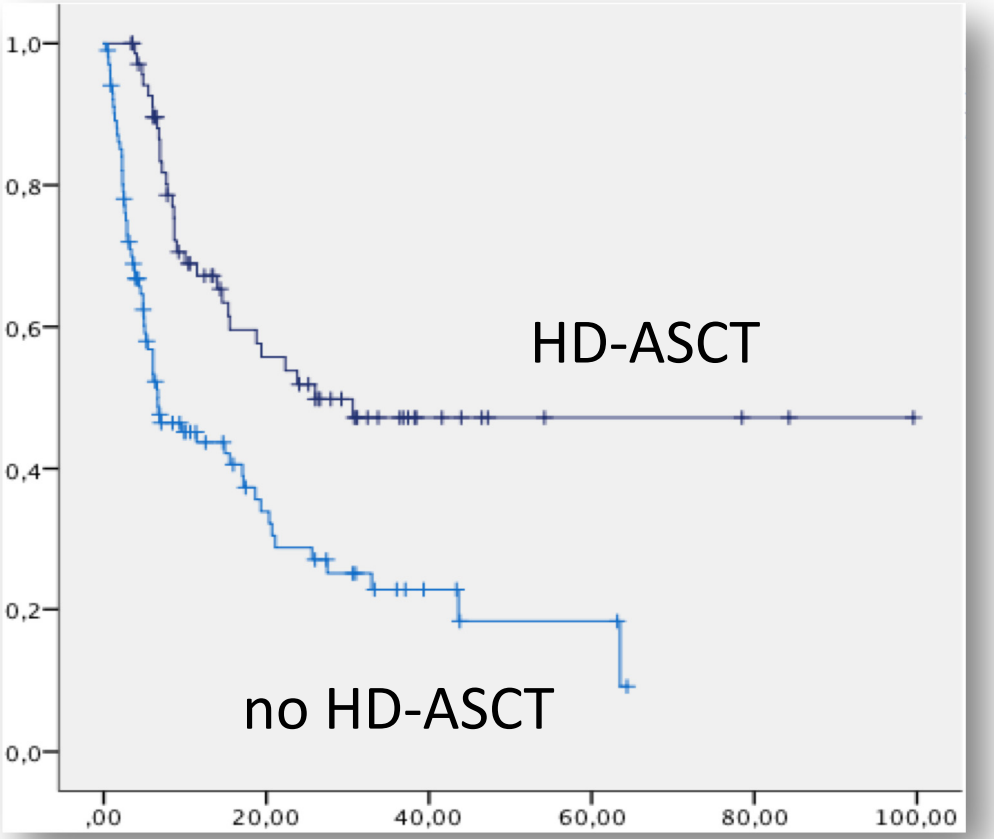
Results

- Median PFS: 7.9 months (95% CI 6.1-9.7)
- Median OS: 14.5 months (95% CI 8.1-21.0)

SCNSL-Register

Results

- Median PFS: 7.9 months (95% CI 6.1-9.7)
- Median OS; 14.5 months (95% CI 8.1-21.0)



Patients receiving HD-ASCT (n=56) median OS: 30 months.

Temozolomid bei relabierten/refraktären primären vitreo-retinalen Lymphomen (R/R PVRL)

- Einfaches, günstiges und gut verträgliches Behandlungsprinzip

Abstract 215

Temozolomide in relapse/refractory primary vitreo-retinal lymphoma (R/R PVRL): a simple, cheap, effective and well tolerated treatment. Result of the largest study on R/R PVRL, from the LOC network

Sylvain Choquet[1], M.Baron[1], A. Lavaud[1], C.Soussain[2], M.Legarff[1], M. Costopoulos[1], K. Maloum[1], C.Houiller[1], E.Gyan[3], P.Soubeyran[4], M.Ertault de la Bretonniere[3], N.Cassoux[1], V.Touitou[1], C.Fardeau[1], D.Roos Weil[1] ,V.Leblond[1] and Khe Hoang-Xuan[1]

[1] APHP Hôpital Pitié-Salplétrière, Sorbonne Université, Paris, France, [2] Hôpital René Huguenin, SaintCloud, France, [3] Hôpital Bretonneau Tours, France, [4] CHUDe Bordeaux, Bordeaux, France

Ocular lymphoma (R/R PVRL)

Background

- rare disease with poor prognosis and high level of relapse, especially in brain
- It often arises in elderly patients

Different classical treatments:

- local treatment (ocular radiotherapy, intra-ocular methotrexate)
- systemic chemotherapy (methotrexate, AraC, ifosfamide ...)
- immunomodulatory drugs (lenalidomide, ibrutinib) under evaluation
- autologous hematopoietic stem cell transplantation (ASCT)

Ocular lymphoma (R/R PVRL)

Methods

- Retrospective and multicentric study
- R/R PVRL and/or patients not eligible for iv chemotherapy
- Temozolomide 150 or 200 mg/m^2, 5 days every 4 weeks, orally,

Ocular lymphoma (R/R PVRL)

Characteristics

Median age : years (ranges)	73 (33-90)
Female sex: n (%)	15 (71)
Cerebral localization at treatment by TZ: n (%)	1 (5)
Median number of lines of treament before TZ : n (ranges)	1 (0-4)
Number of patients treated by ASCT before TZ: n(%)	2 (10)
Number of patients treated by Len or Ibru before TZ: n (%)	Len 1 ibru 2
ECOG = 0: n (%)	17 (94)
Median duration of TZ treatment: months (range)	5,2 (1-40)

Two patients were treated in first line by temozolomide, they were 85 and 89 y old

Toxicity

Grade 3-4 neutropenia: n (%)	2 (10)
Grade 3-4 thrombopenia: n(%)	1 (5)
Grade 3-4 anemia: n(%)	1 (5)
Grade 3 nauseas: n (%)	2 (10)
Asthenia: n (%)	1 (5)
Liver toxicity: n(%)	**0**
Secondary cancers: n(%)	**0**
Treatment related deaths: n (%)	**0**

Ocular lymphoma (R/R PVRL)

Results:

- Median follow-up: 42 mo
- ORR: 81% CR: 71%
- Median duration of response: 10,9 months (3-115)
- Median duration of response if CR: 55 months

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Results:

- Median follow-up: 42 mo
- ORR: 81% CR: 71%
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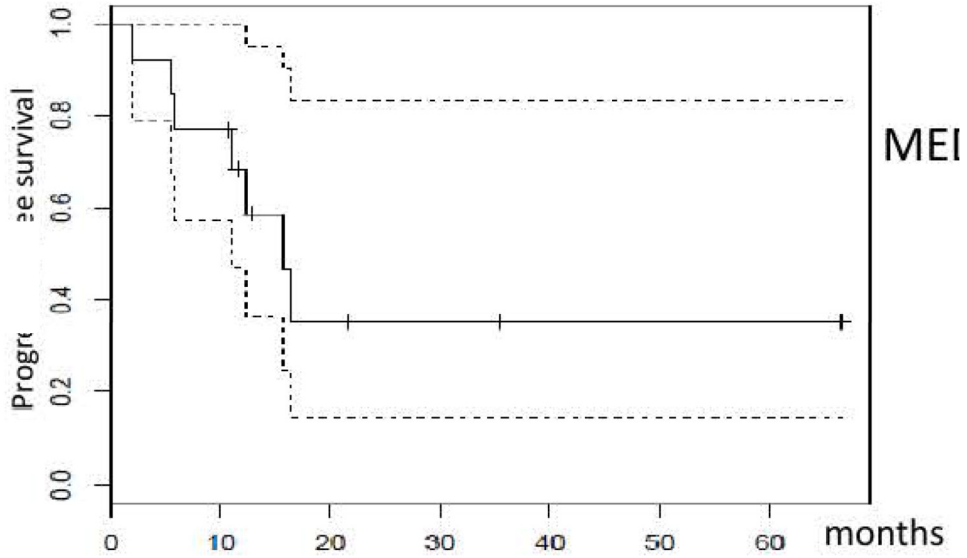
- Median duration of response if CR: 55 months

- Median PFS: 12 mo
- Median OS: NR



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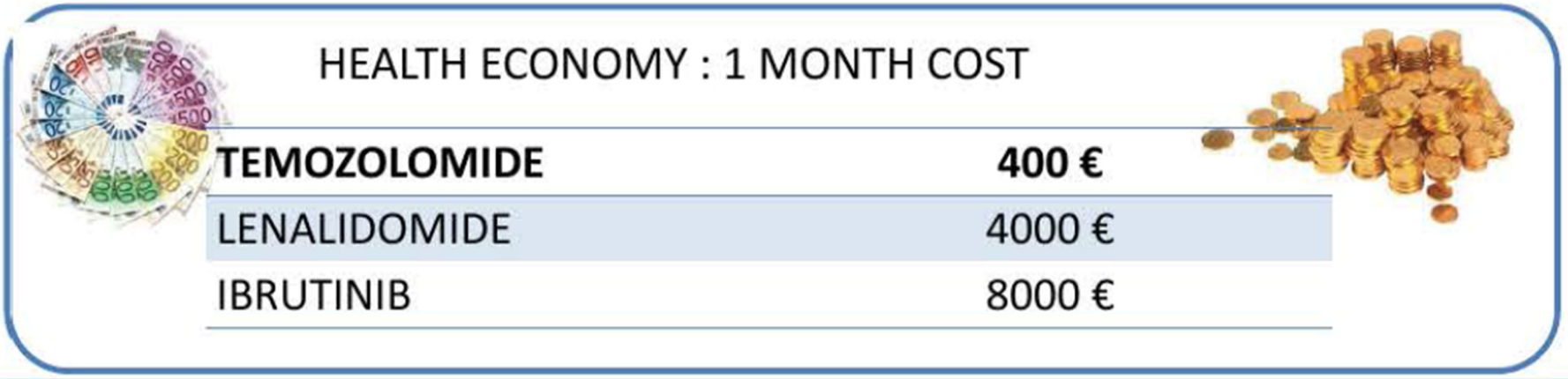

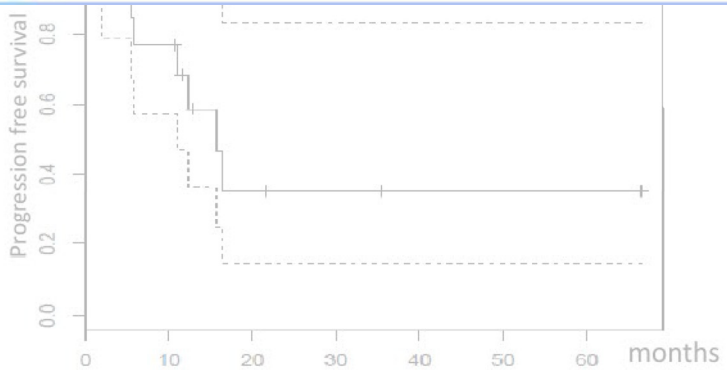

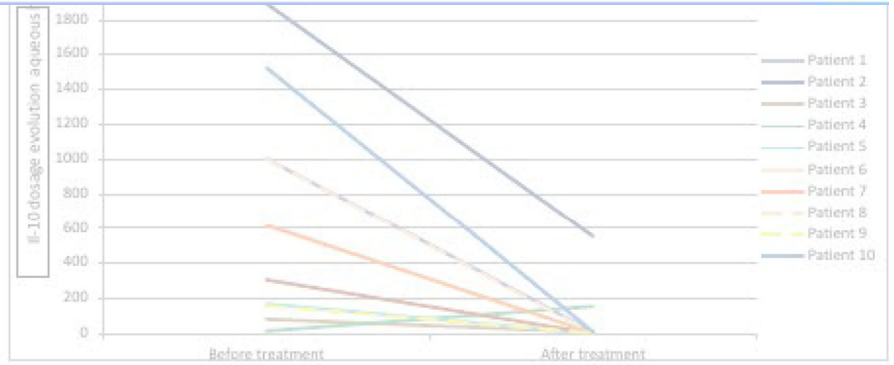

15. ICML - Take-Home messages:

Erstlinientherapie Ältere Patienten:

- Hochdosistherapie machbar und effektiv
- CAVE! Toxizität bei älteren Patienten – gute Überwachung nötig

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Rezidivtherapie bei PCNSL:

- Interessante Daten zu R-CHOP + mod. TNF
- Wird alles ganz einfach?

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SCNSL-Register:

- Ohne HDT/ASCT sehr schlechte Prognose

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Intraokuläre Lymphome:

- Temozolomid: einfach, effektiv und günstig

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- CAVE! Toxizität bei älteren Patienten – gute Überwachung nötig

Rezidivtherapie bei PCNSL:

- Interessante Daten zu R-CHOP + mod. TNF
- Wird alles ganz einfach?

SCNSL-Register:

- Ohne HDT/ASCT sehr schlechte Prognose

Intraokuläre Lymphome:

- Temozolomid: einfach, effektiv und günstig

CAR-T-Zellen bei SCNSL → Bericht Peter Borchmann vom EHA

- *Feasible without excess NT and with high response-rates (Liso-cel)*

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT 15-ICML 18.–22. Juni 2019

Die Kurzpräsentationen sind online unter

www.lymphome.de/15-icml

Für den Inhalt verantwortlich:

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Diese hatten keinen Einfluss auf die Inhalte.