

Lymphom
Kompetenz
KOMPAKT



KML KONGRESSE

Expert:innen berichten zu
Lymphomen & Leukämien



18th ICML LUGANO

17. – 21. Juni 2025



Prof. Dr. med. Klaus Herfarth
Universitätsklinikum Heidelberg

Radiotherapie bei Lymphomen

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ICML 2025 LUGANO, Italien wird in Kooperation mit fünf unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	-
Beratungs-/ Gutachtertätigkeit	-
Besitz von Geschäftsanteilen, Aktien oder Fonds	-
Patent, Urheberrecht, Verkaufslizenz	-
Honorare	-
Finanzierung wissenschaftlicher Untersuchungen	Roche Pharma
Andere finanzielle Beziehungen	-
Immaterielle Interessenkonflikte	-

Kapitel 1

Niedrigdosis Bestrahlung bei indolenten Lymphomen

Local control with response-adapted very low dose radiotherapy (RA-VLDRT) of 4 Gy for indolent non-Hodgkin lymphoma

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Department of Radiation Oncology, Memorial Sloan Kettering Cancer

Nikhil P. Mankuzhy, Brandon S. Imber, Jasme Lee, Paige Pammer, Beatrice Fregonese, Adriana Cajo, Gustav Cederquist, Alexandra D. Dreyfuss, Kaitlyn Lapen, Roshal R. Patel, Zachary R. Moore, Carla Hajj, Andrew D. Zelenetz, Zhigang Zhang, Gilles A. Salles, Joachim Yahalom



Memorial Sloan Kettering
Cancer Center

18 June 2025



Abtrakt 108

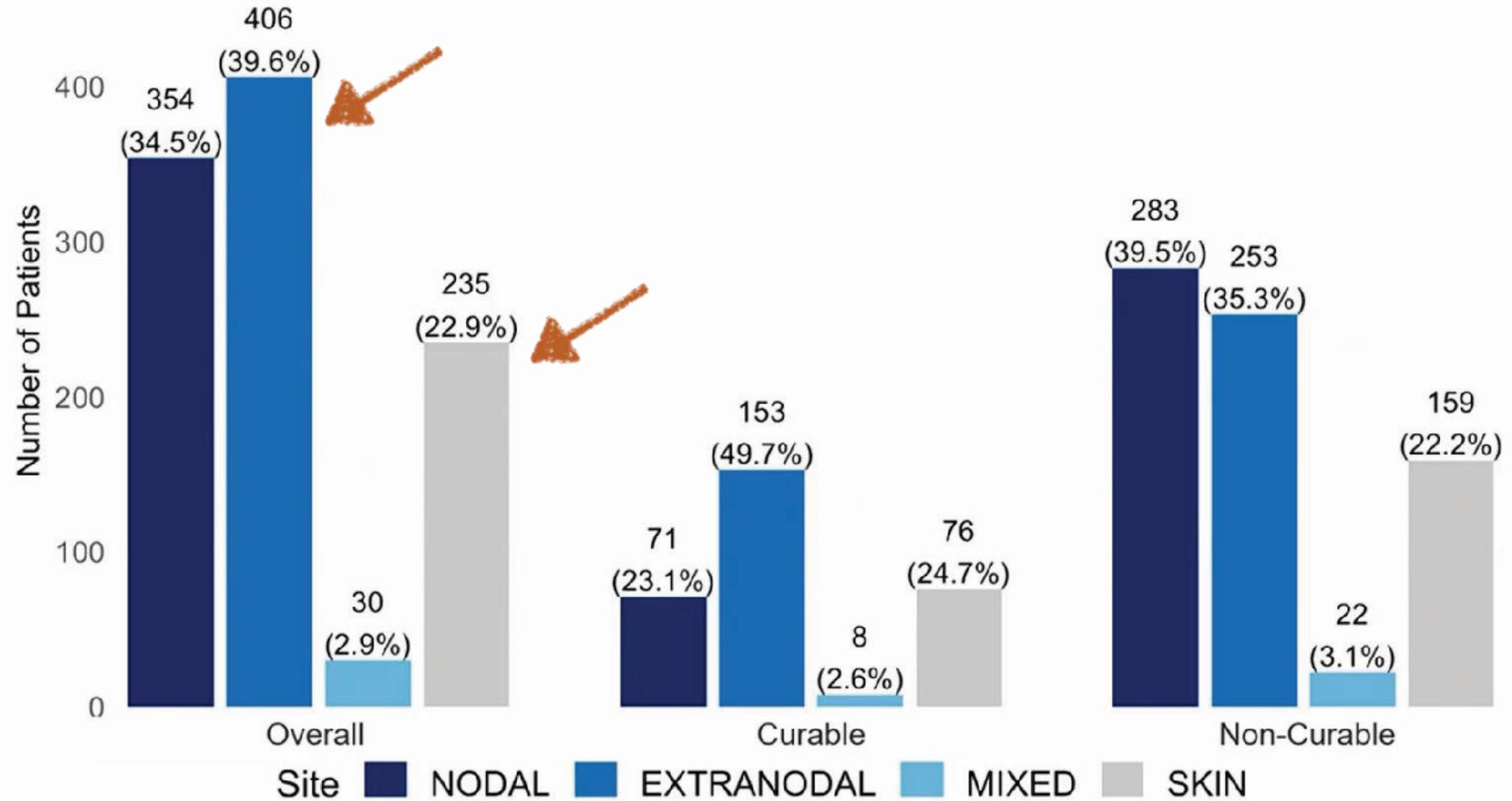
Results: Summary of lesion characteristics

Characteristic	Overall N = 1025	Curable N = 308 (30%)	Non-Curable N = 717 (70%)
VLDRT Dose			
2 Gy x 2	772 (75%)	226 (73%)	546 (76%)
4 Gy x 1	253 (25%)	82 (27%)	171 (24%)
Lesion Excised	21 (2.0%)	16 (5.2%)	5 (0.7%)
SUV (IQR)	6.3 (4.1, 9.5)	5.2 (3.2, 7.4)	6.7 (4.4, 10.1)
Diameter (cm, IQR)	2.5 (1.8, 3.9)	2.1 (1.60, 3.1)	2.7 (1.9, 4.1)

Pathology at VLDRT	Overall N = 1025	Curable N = 308 (30%)	Non-Curable N = 717 (70%)
FL (non-skin)	484 (47%)	106 (34%)	378 (53%)
MZL (non-skin)	245 (24%)	113 (37%)	132 (18%)
SLL/CLL	22 (2.1%)	0 (0%)	22 (3.1%)
iNHL NOS (non-skin)	39 (3.8%)	13 (4.2%)	26 (3.6%)
Cutaneous iNHL	235 (23%)	76 (25%)	159 (22%)

Abtrakt 108

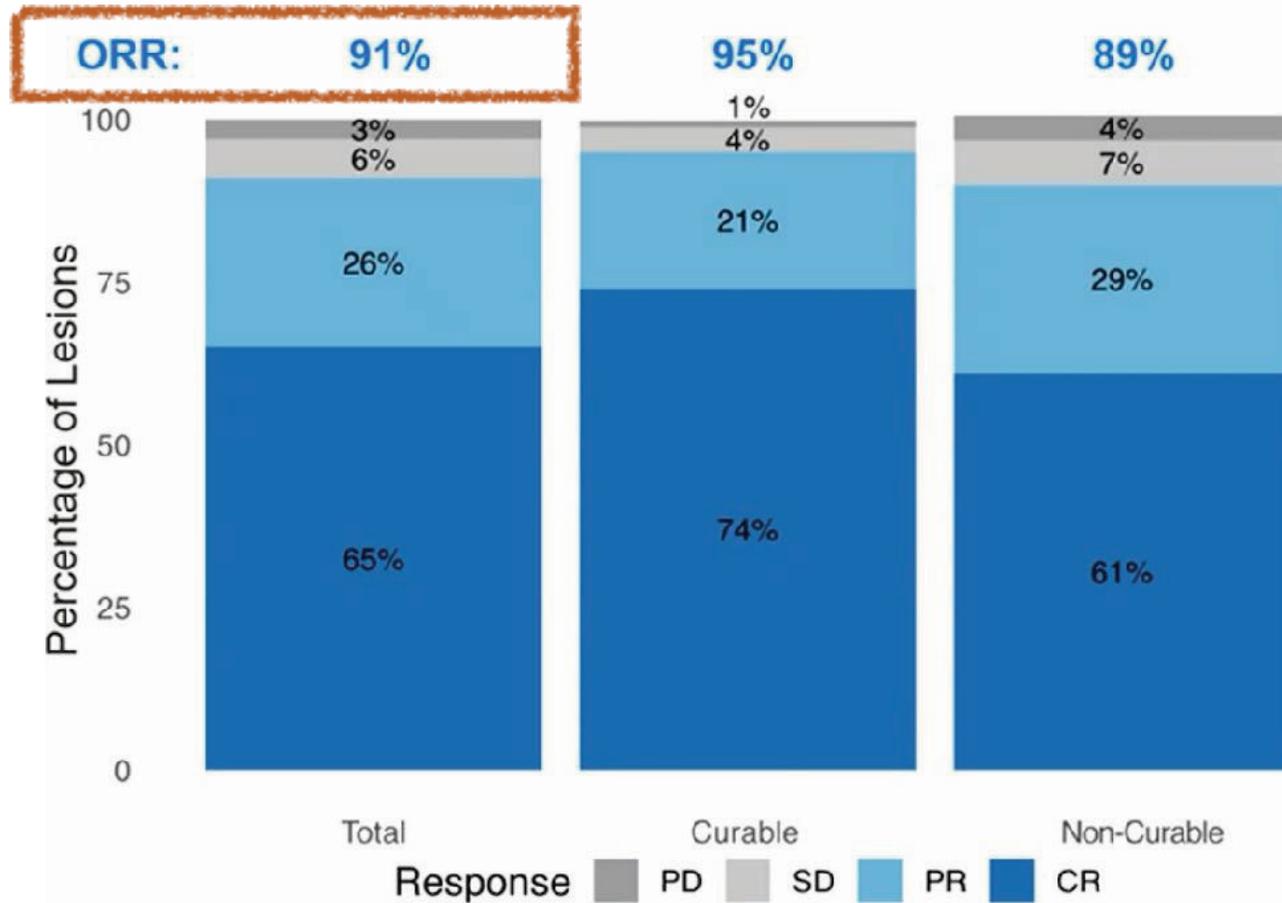
Results: Summary of lesion characteristics



Abtrakt 108

Results: Response rate at early response assessment (ERA)

ERA done at 10.4 weeks (IQR 8.4-13) using PET in 67%



Comparison of ORR (CR/PR)

Curable (95%) vs Non-Curable (89%):
 $p = 0.003$

Non-skin: FL (89%) vs MZL (94%):
 $p = 0.046$

2 Gy x 2 (91%) vs 4 Gy x 1 (91%):
 $p > 0.9$

UVA: Odds of Complete Response

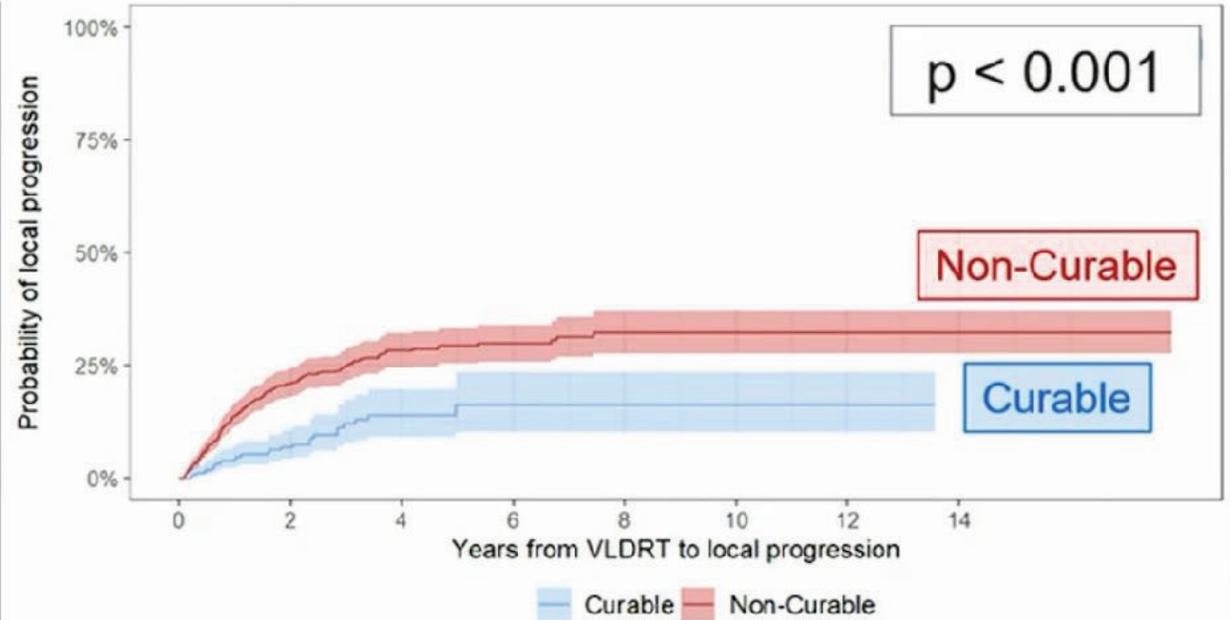
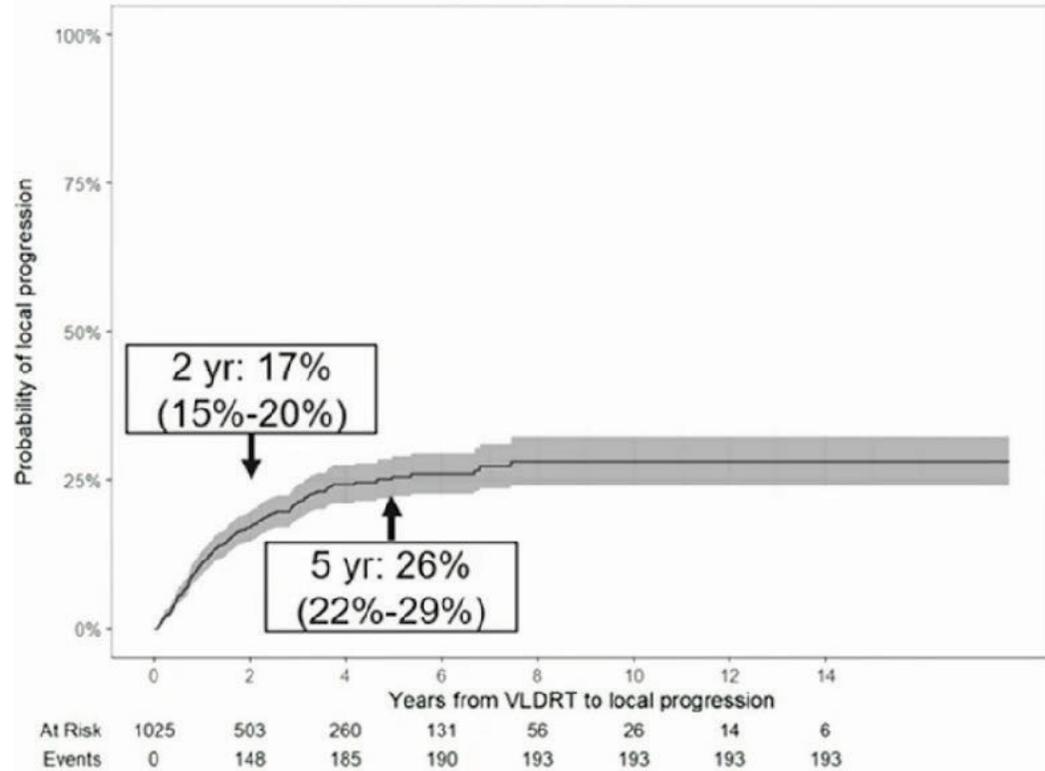
↓ Stage*, SUV >10, >6cm*, SLL/CLL*, prior systemic therapy, prior- anti-cD20 therapy*

↑ Cutaneous*

*significant on MVA

Abtrakt 108

Results: Cumulative incidence of local progression



Curable		308	147	66	28	8	3	1	0
At Risk	Events	0	16	25	26	26	26	26	26
Non-Curable		717	356	194	103	48	23	13	6
At Risk	Events	0	132	160	164	167	167	167	167

Abtrakt 108

Ultra-low dose radiotherapy (4Gy) for indolent orbital adnexal lymphomas (IOAL):

An International Lymphoma Radiation Oncology Group study

Andrew Wirth (on behalf of Lilly Shen)
Peter MacCallum Cancer Centre, Melbourne

Lilly Shen, Brandon Imber, Chelsea Pinnix, Joachim Yahalom, Adriana Cajo, Jillian Gunther, Timothy Lin, Michael MacManus, Mathias Bressel, Mario Levis, Umberto Ricardi, Christine Holloway, Andrea Ng, Louis Constine, Terri Igwe, Daniel Huang, David Hodgson, Ying Ying Sum, John Plastaras, Jonathan Baron, Margaret Harris, Tim Illidge, Senzo Taguchi, Masahiko Oguchi, Jessica Brady, George Mikhaeel, Yolanda Tseng, Sidney Davis, Khaled Elsayad, Hans Eich, Michael Binkley, Ayes Hahashmi, Leslie Ballas, Yeoh Kheng, Iris Sin, Andrew Wirth



Australasia

Alfred health
Cancer Institute Hospital of JFCR
Peter MacCallum Cancer Centre
Singapore Cancer Centre

Europe/UK

Christie Hospital
Guys and St Thomas
University of Turin
University Hospital Muenster

North America

Dana Farber Cancer Institute
Hospital of the University of Pennsylvania
Memorial Sloan Kettering Cancer Centre
MD Anderson Cancer Centre
Princess Margaret Cancer Centre
Rutgers Cancer Institute of New Jersey
Stanford Cancer Centre
University of British Columbia
University of Southern California
University of Rochester Medical Centre
University of Washington Cancer Centre
Washington University St Louis

Patient characteristics

Current analysis 318 Orbits, 268 patients*

Median age: 68 years (range 22-97)

Sex: 56% females

Prior lymphoma history: 33%

Localised disease at time of orbit RT: 54%

Biopsy 86%

Clinical/Radiological features + history indolent NHL 14%

***data collection ongoing – not final results**

Response rate (all results per orbit)

Response was assessed* at a median of 81 days post RT

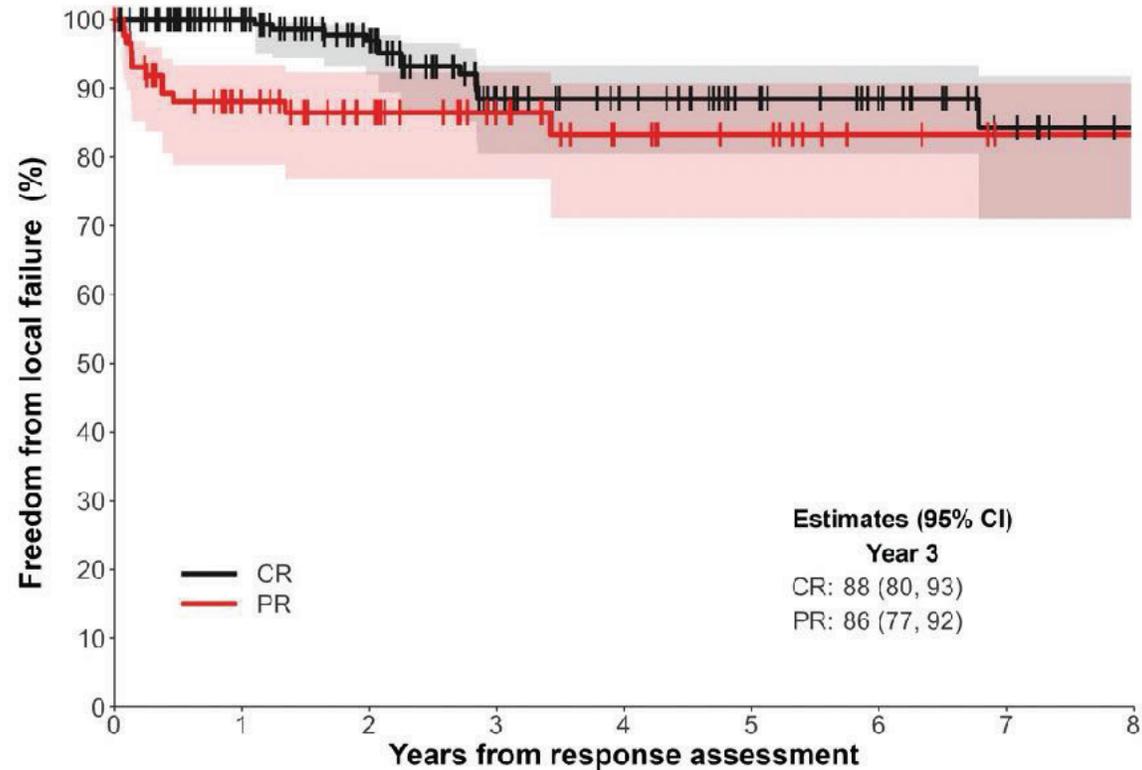
(307 / 318 orbits evaluable)

Initial response	
CR	64%
PR	32%
<PR	4%

*Not rigorous in all cases

Structural imaging	41%
Ophthalmologist review	37%
Routine clinic review	32%

Landmark analysis by initial response*



* Assessment not rigorous in all cases

No. at risk (No. events)

	0	1	2	3	4	5	6	7	8
CR	184 (0)	149 (0)	115 (4)	66 (12)	53 (12)	40 (12)	30 (12)	19 (13)	13 (13)
PR	93 (0)	60 (10)	46 (11)	31 (11)	22 (12)	16 (12)	9 (12)	6 (12)	6 (12)

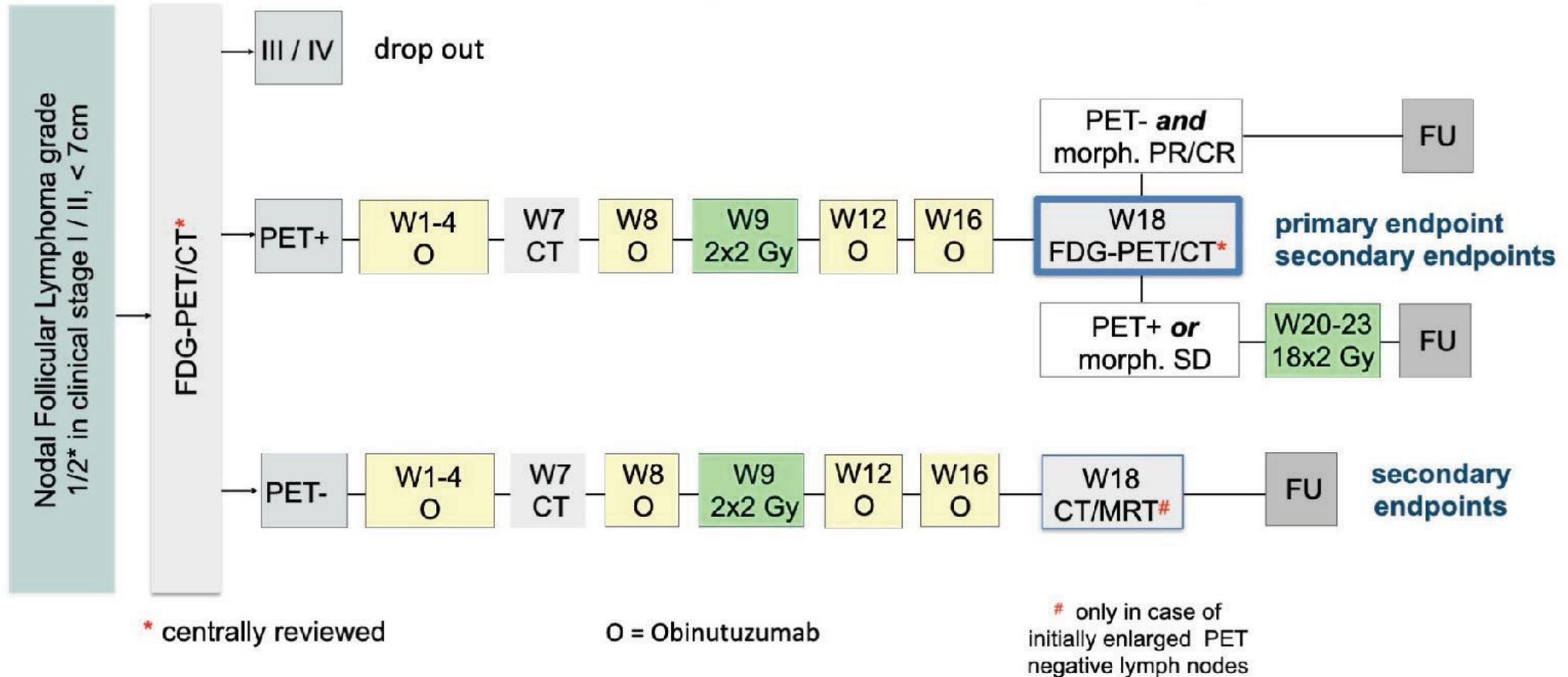


High PFS with low infield recurrences after low dose radiotherapy and Obinutuzumab in early stage nodal follicular lymphoma: final results of the GAZAI study (GLA 2018-3)

Klaus Herfarth, Christian W. Scholz, Kai Hübel, Stefan Wirths, Christian Buske, Julia v. Tresckow, Roswitha Forstpointner, Simon Heidegger, Georg Lenz, Laila König, Julia Meißner, Laila König, Ulrike Höller, Christian Baues, Chiara De-Colle, Thomas Wiegel, Thomas Gauler, Minglun Li, Stephanie E Combs, Hans Eich, Paul Thalmann, Eleni Mavriopoulou, Christiane Pott and Martin Dreyling

Abstrakt 110

GAZAI (04/18 - 11/21)



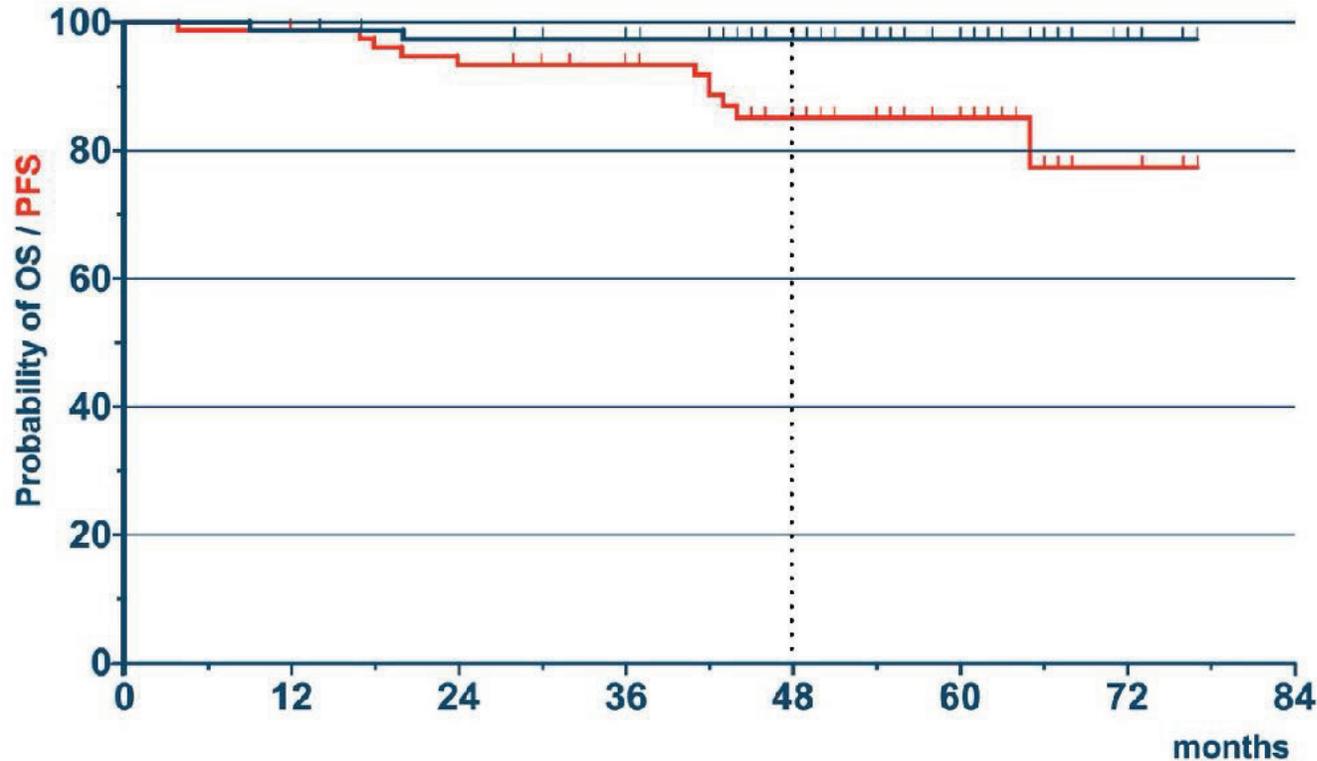
Response

metabolic			morphologic	
	w 18	DS		w 18
CR	46 (87 %)	1/2	CR/CRu	49 (91 %)

Herfarth et al. ICML 2023

3 / 6 patients with mPR received Salvage RT

OS / PFS



- Median f/u 49 months
- OS (4 yrs) 97%
- PFS (4 yrs) 85%
- 10 recurrences after median 41 months

Recurrences

- Relation to RT volume
- initial stage

inside	i/o	outside
1	2*	7

Io	I	II
0 / 24	4 / 24	6 / 30

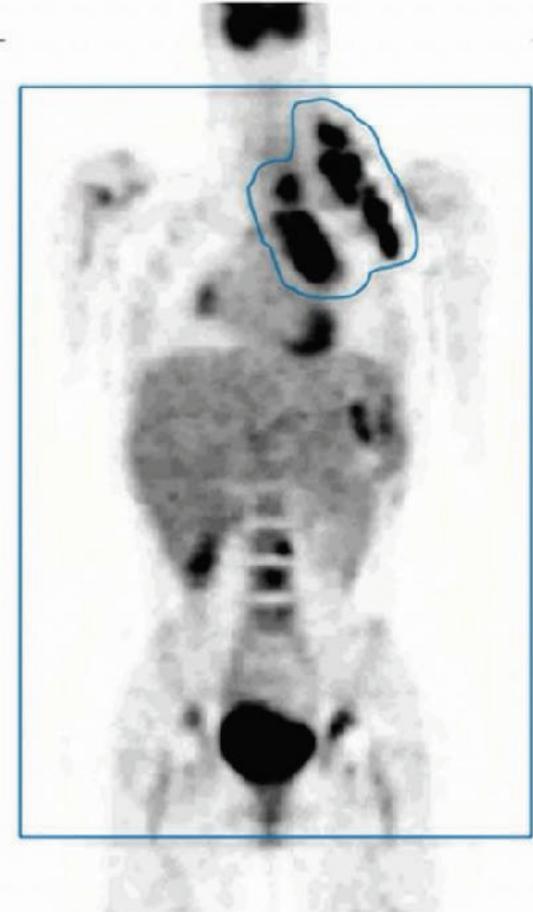
* 1 patient with salvage RT in week 22-24

Kapitel 2

Bridging / Debulking / Priming CAR-T-Zell Therapie

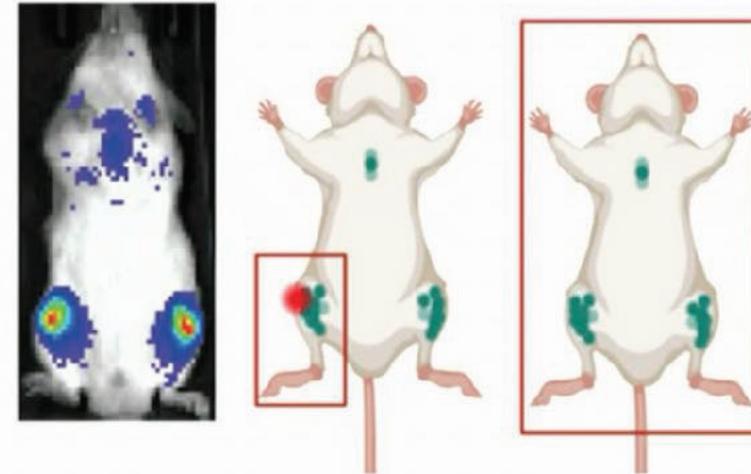
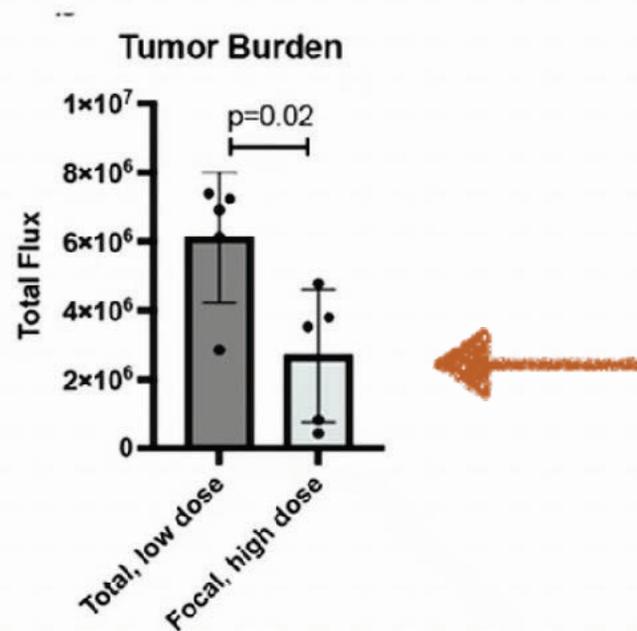
Clinical Relevance

- You have a patient going into CAR T-cells, who you know is unlikely to respond
 - E.g., high disease burden, multiple locations
- Is it better to use a higher dose to focal bulky disease, or low dose to a wide area?
- IF there is synergy between low dose radiation and CAR T-cells, what is the mechanism?



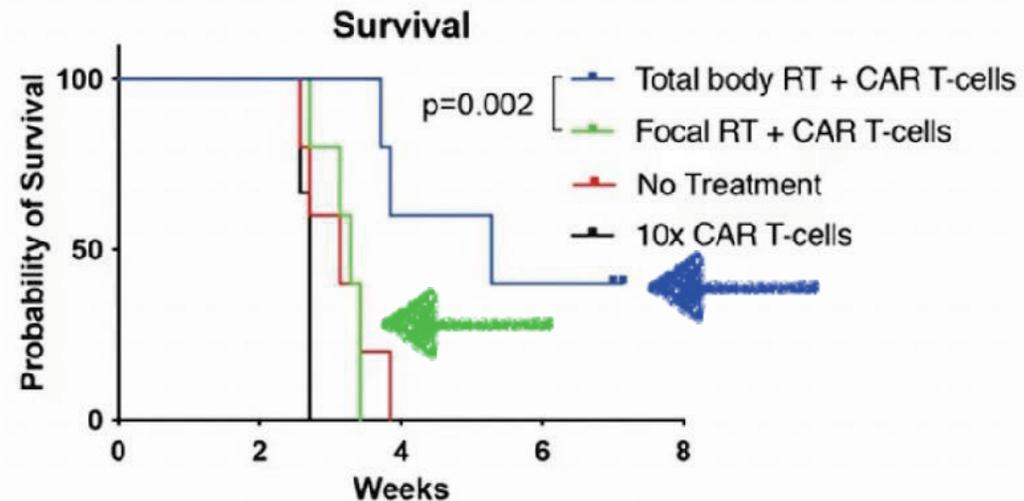
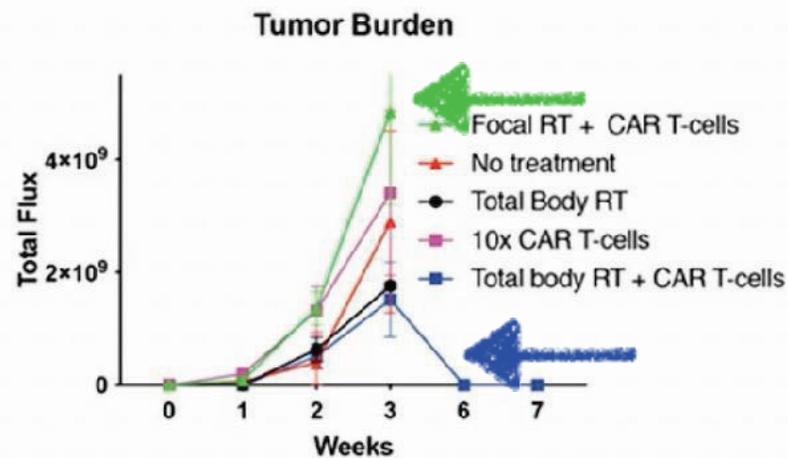
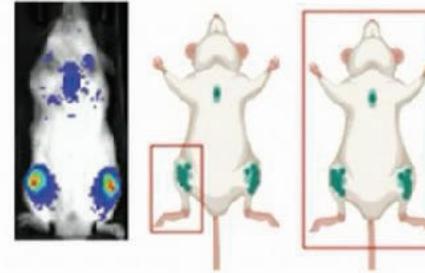
High dose focal RT is more systemically debulking than 1.8 Gy TBI

- 4 Gy x 5 to the leg, or
- 1.8 Gy x 1 to the whole body



Low dose TBI improves CAR T efficacy more than focal debulking

- 4 Gy x 5 to the leg, or
- 1.8 Gy x 1 to the whole body



Kim et al, *Blood Advances* 2023

Conclusions

- 2 Gy TTI leads to significantly better survival than selective tumor debulking with higher dose
 - Irradiated tumor cells are more susceptible to being killed by CAR T-cells for a window of time (Kim et al, *Blood Advances* 2023)
- Tumor induces metabolic dysfunction in CAR T-cells
 - Tumor releases phosphoethanolamine; this consumes DAG in T-cells, which is required for TCR and CAR signaling
- Tumor induced CAR T-cell metabolic dysfunction is long lasting, impairing ability to kill future tumor cells
- Low dose tumor irradiation reduces phosphoethanolamine production by tumor cells, leading to improved CAR T-cell function

Phase I Study of Split-Course Bridging Radiotherapy (SC-BRT) Prior to CAR T-Cell Therapy for Relapsed/Refractory B-Cell Lymphomas

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*equally contributing author



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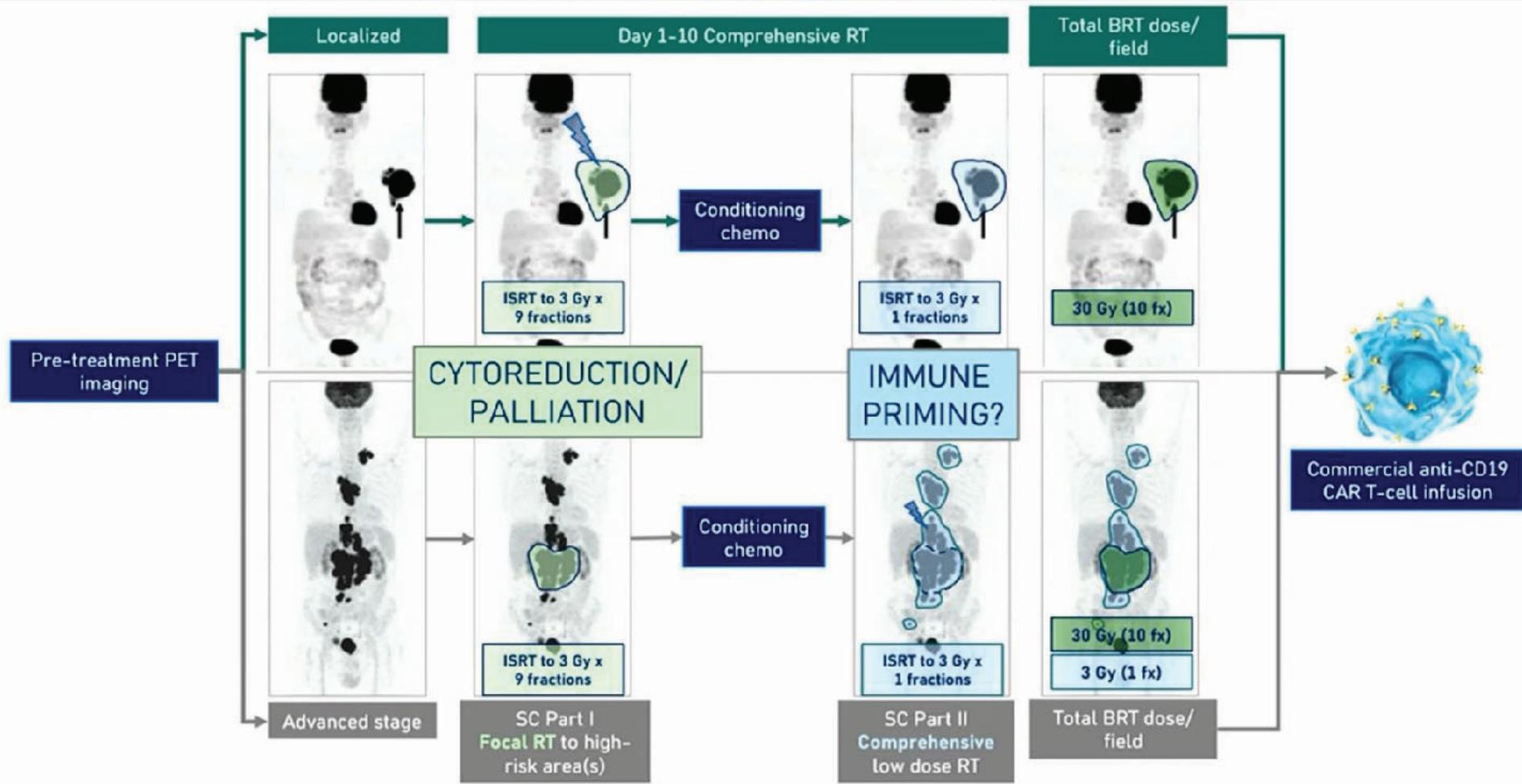


Wednesday, 18 June 2025
FOCUS ON RADIATION THERAPY
17:40 – 17:50

Abstrakt 112

We developed a strategy called split course bridging RT (SC-BRT)

Stage-adapted, split course bridging radiotherapy program (SC-BRT)



Abstrakt 112

Primary endpoint: safety within 30d of CAR T infusion



Feasibility

All successfully received SC-BRT followed by standard lymphodepletion and commercial CD19 CAR T



How to approach intercurrent progression of disease on pre-Phase II PET



Safety

1/20 severe toxicity events*
Grade 5 CRS at day +6 in medically comorbid patient with high burden of kinetically active disease receiving axi-cel

*Otherwise SC-BRT well-tolerated with grade 1-2 BRT-related toxicities

Cytokine release syndrome (CRS)

Overall incidence	13/20 (65%)
Grade 1	7
Grade 2	5
Grade 5	1

Immune effector cell-associated neurotoxicity syndrome (ICANS)

Overall incidence	2/20 (10%)
Grade 1	0
Grade 2	1
Grade 3	1

Alle Kurzpräsentationen sind online unter

www.lymphome.de/icml2025

Für den Inhalt verantwortlich:

Prof. Dr. med. Klaus Herfarth

Universitätsklinikum Heidelberg

Lymphom Kompetenz KOMPAKT



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Das Informationsprojekt wird unterstützt von:

abbvie



Lilly

Die Firmen hatten keinen Einfluss auf die Inhalte.