



# IORT combined with immunotherapy in brain metastases

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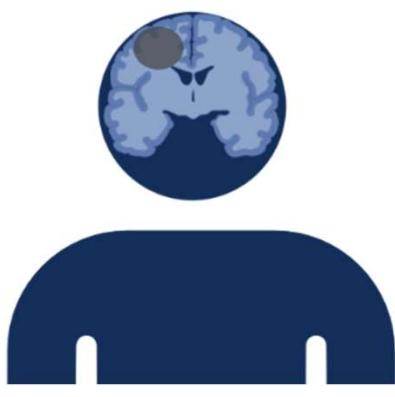
November 08, 2024



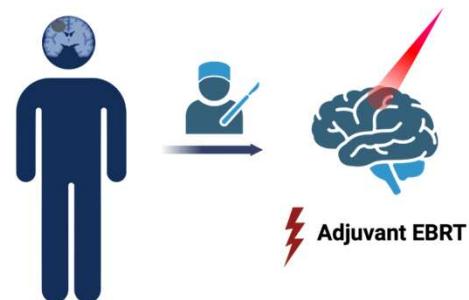
**Ukb** universitäts  
klinikum bonn



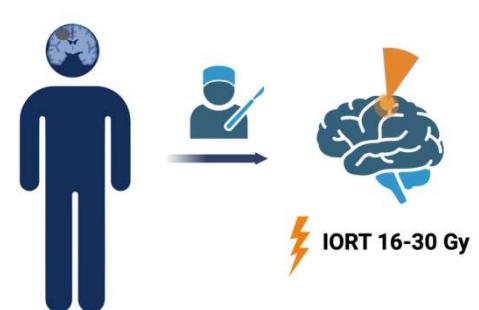
# Background



Brain metastases



Adjuvant EBRT

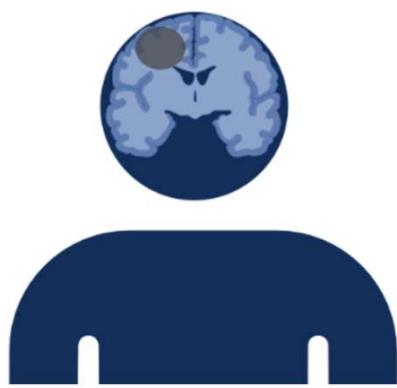


IORT 16-30 Gy

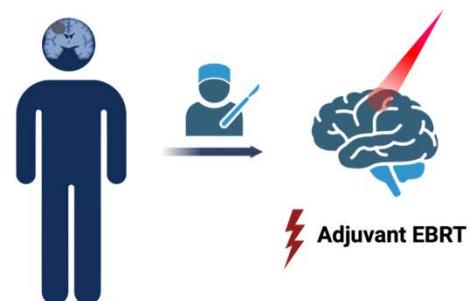
Immediate tumor cell eradication



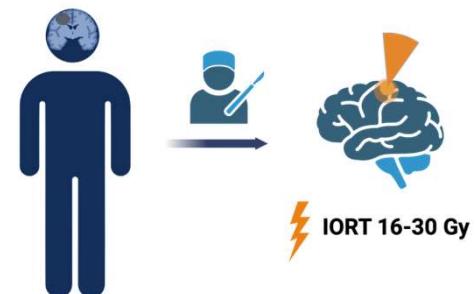
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Brain metastases

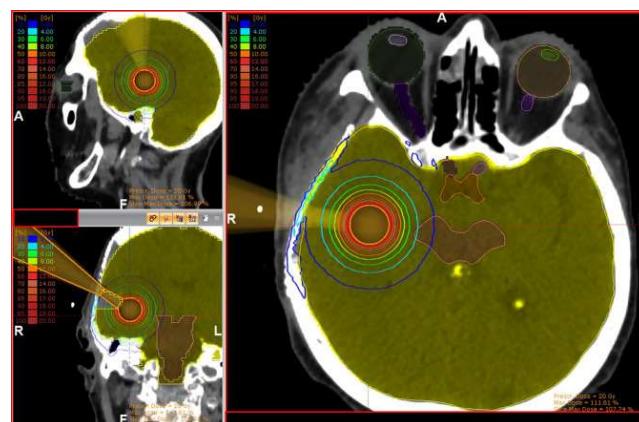


Adjuvant EBRT



IORT 16-30 Gy

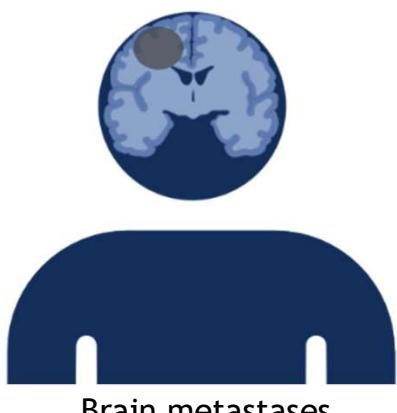
Immediate tumor cell eradication  
Superior organ-at risk preservation



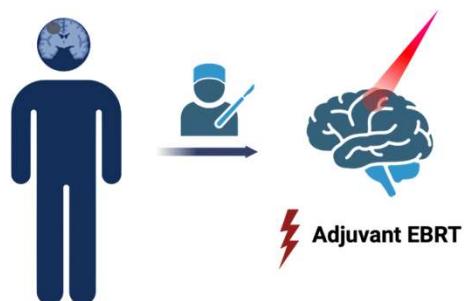
Sarria et al., 2021

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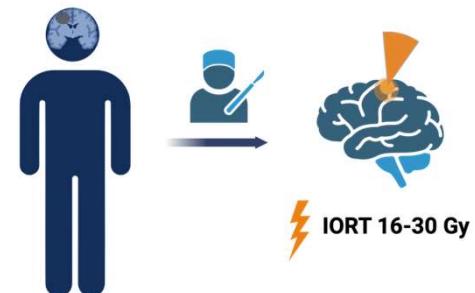
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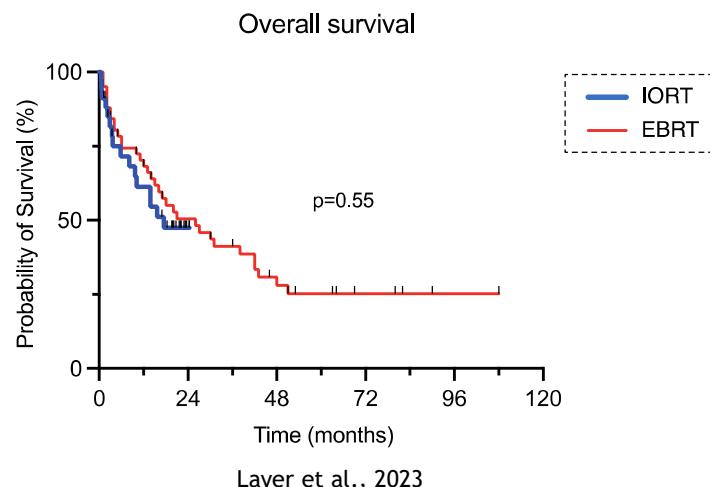
Brain metastases



Adjuvant EBRT

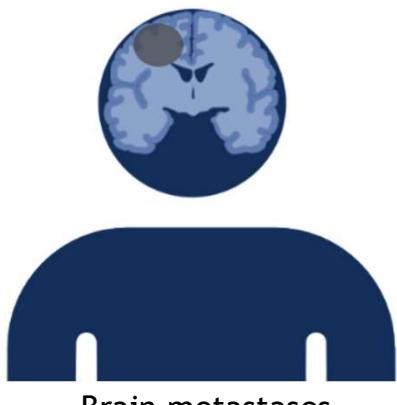


IORT 16-30 Gy

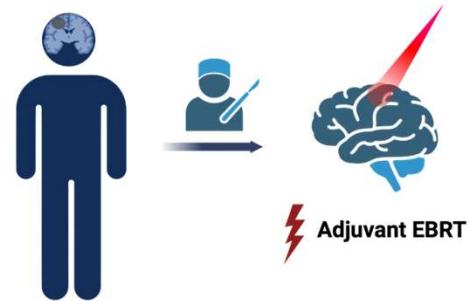


Immediate tumor cell eradication  
Superior organ-at risk preservation  
**Equal clinical outcomes**

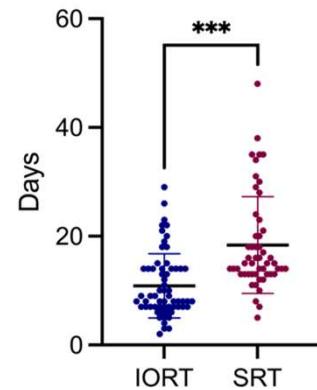
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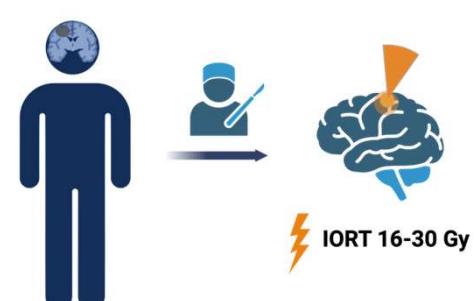
Brain metastases



Total in-hospital times



Dejonckheere et al., 2023



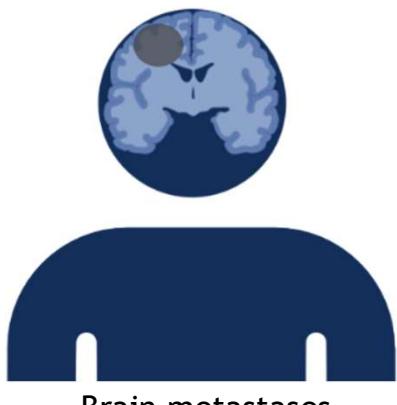
Immediate tumor cell eradication

Superior organ-at risk preservation

Equal clinical outcomes

**Reduced hospitalization times**

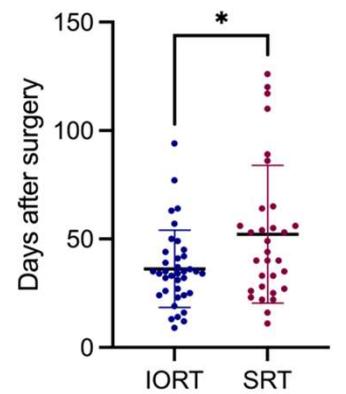
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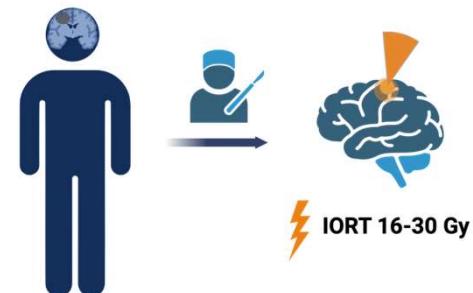
Brain metastases



Time to next treatment

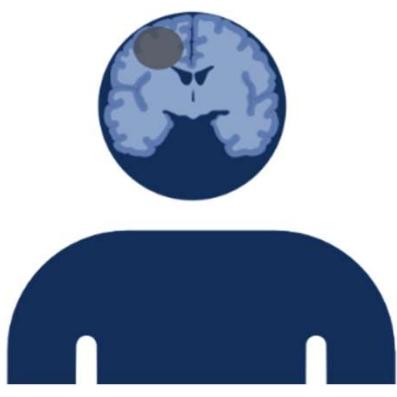


Dejonckheere et al., 2023

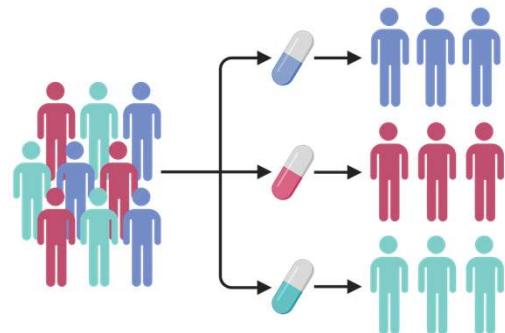
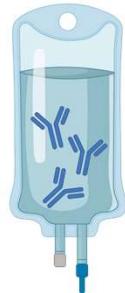
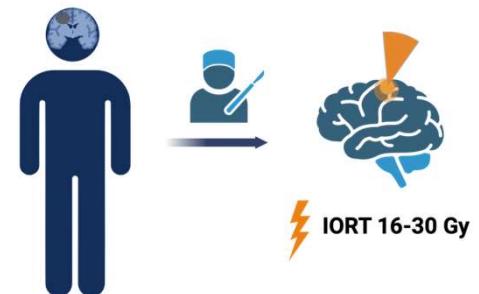
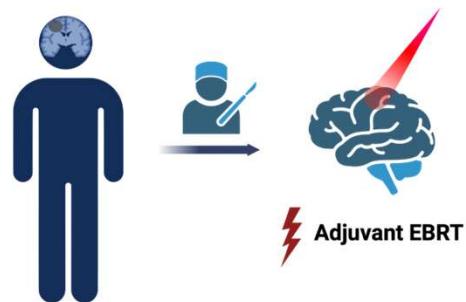


- Immediate tumor cell eradication
- Superior organ-at risk preservation
- Equal clinical outcomes
- Reduced hospitalization times
- Timely admission to subsequent treatments**

# Background



Brain metastases



Immediate tumor cell eradication

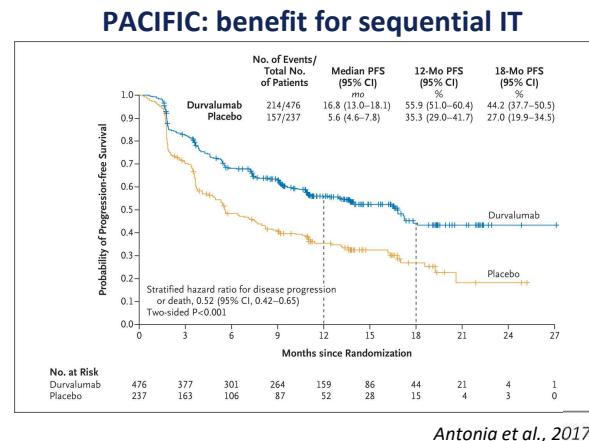
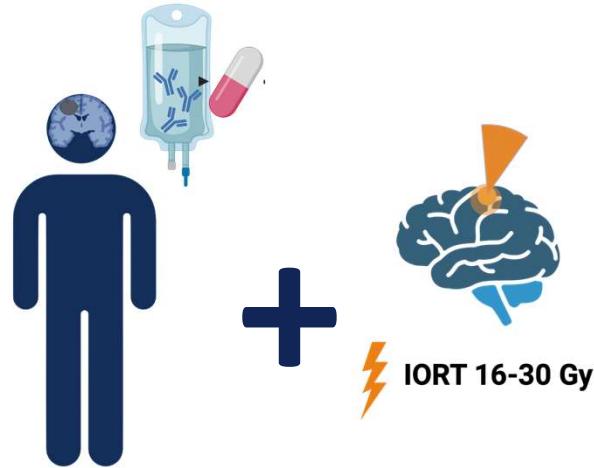
Superior organ-at risk preservation

Equal clinical outcomes

Reduced hospitalization times

Timely admission to subsequent treatments

# Timing matters



Efficacy

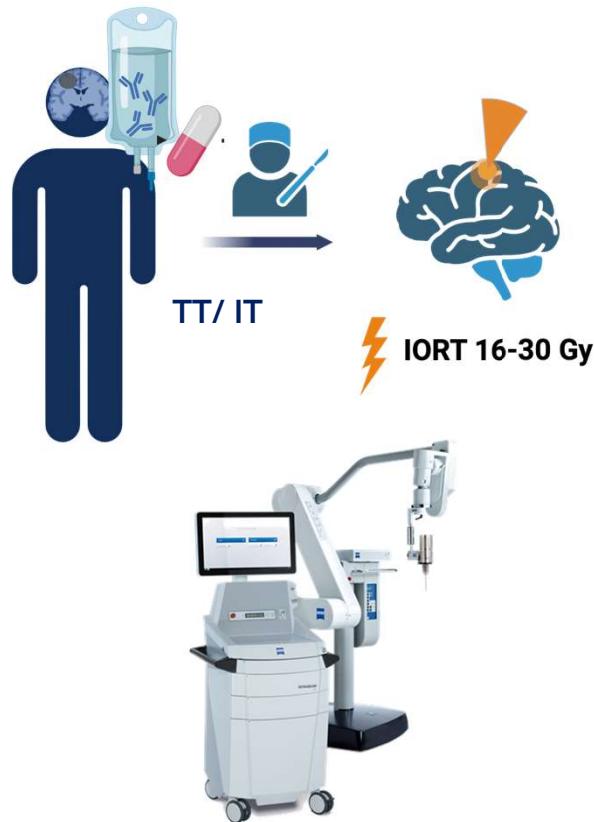
Timing

Toxicity

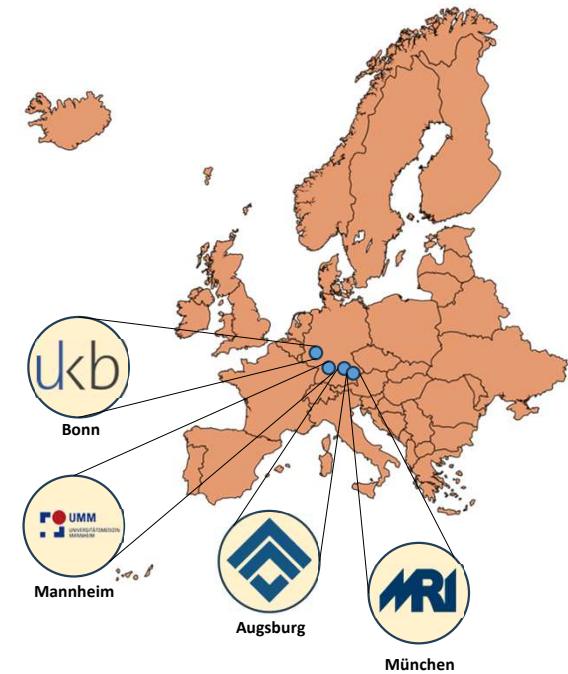


# Study Design

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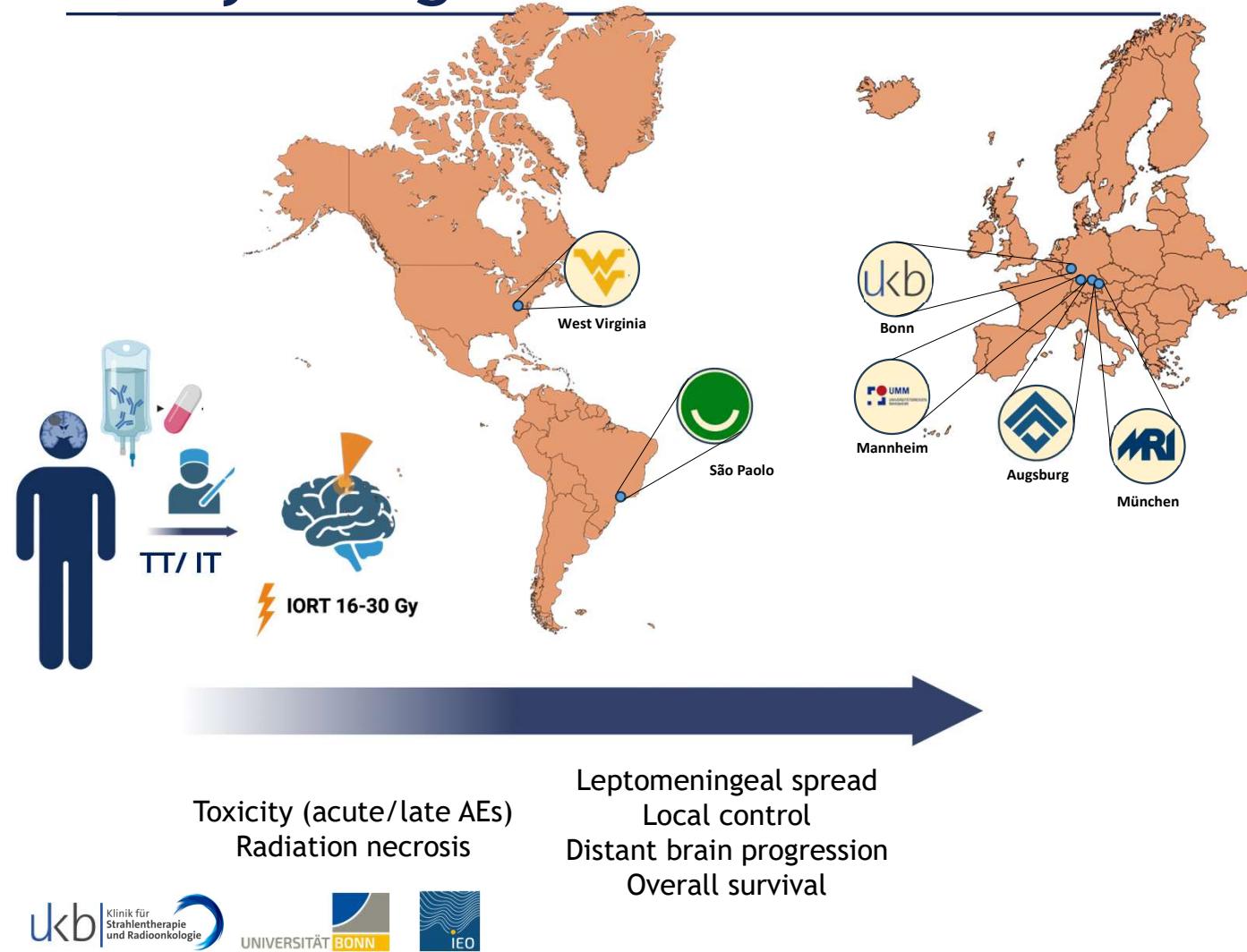


INTRABEAM® (Carl Zeiss Meditech)



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# Study Design

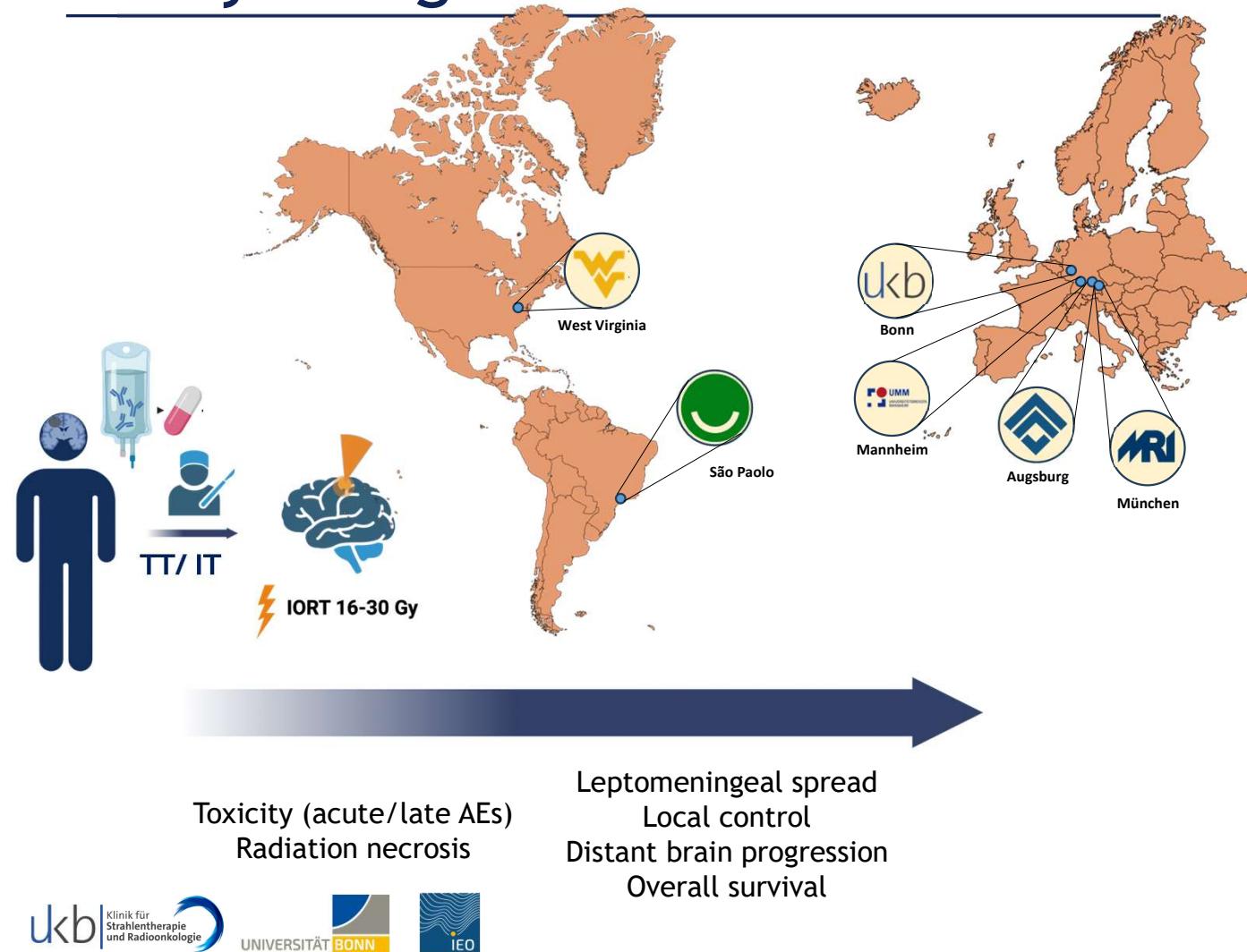


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Variable	n (%)	Median (range)
Gender		
Male	56 (54.4)	
Female	47 (45.6)	
Age (years)		63 (35-85)
Tumor entity		
NSCLC	53 (51.5)	
Melanoma	25 (24.3)	
RCC	13 (12.6)	
Breast	4 (3.9)	
SCLC	3 (2.9)	
Others	5 (4.9)	
Localization		
Frontal lobe	36 (35.0)	
Parietal lobe	28 (27.2)	
Occipital lobe	18 (17.5)	
Temporal lobe	13 (12.6)	
Cerebellum	8 (7.8)	
Max. pre-surgical diameter (mm)		34 (8-70)
Pre-surgical tumor volume (ccm)		22.9 (1.2-701.7)
Multiple BMs		48 (46.6)
Number of BMs		1 (1-16)
RT to other BMs		50 (48.5)
Relevant overlap ( $\geq 10\%$ isodose)		14 (13.6)
Extracranial metastases		66 (64.1)
KPS		80 (40-100)
DS-GPA		2 (0-4)

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# Study Design

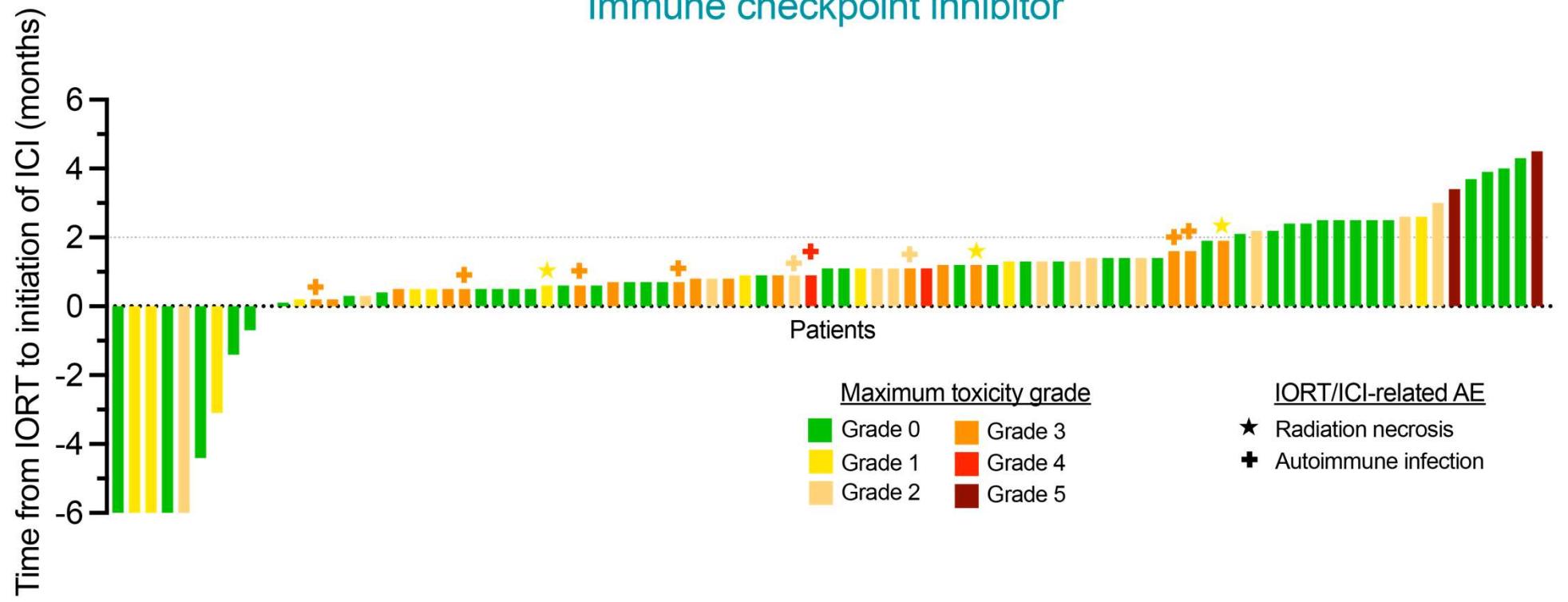


Variable	n (%)	Median (range)
<b>IORT dose (Gy)</b>		25 (16-30)
18	5 (4.9)	
20	40 (38.8)	
24	4 (3.9)	
25	3 (2.9)	
26	1 (1.0)	
30	50 (48.5)	
<b>Applicator diameter (mm)</b>		20 (15-40)
Time 1st diagnosis to IORT (months)		1 (0-297)
<b>Immune checkpoint inhibitor</b>		90 (87.4)*
Pembrolizumab	36 (40.0)	
Ipilimumab + nivolumab	20 (22.2)	
Atezolizumab	16 (15.5)	
Nivolumab	13 (14.4)	
Durvalumab	4 (4.4)	
Ipilimumab	1 (1.1)	
<b>Time from IORT to IT (months)</b>		1.1 (-22.3-34)
<b>Number of IT cycles</b>		6 (1-93)
<b>TT drug</b>		25 (24.3)*
BRAF/MEK inhibitor	6 (24.0)	
TKI	5 (20.0)	
MKI	6 (24.0)	
VEGF targeting*	6 (24.0)	
Androgen deprivation	3 (12.0)	
Anti-Her2neu	3 (12.0)	
Anti-TNFα	1 (4.0)	
<b>Time from IORT to TT (months)</b>		1.2 (-38.9-22.9)
<b>Duration of TT treatment (months)</b>		7 (2-68)

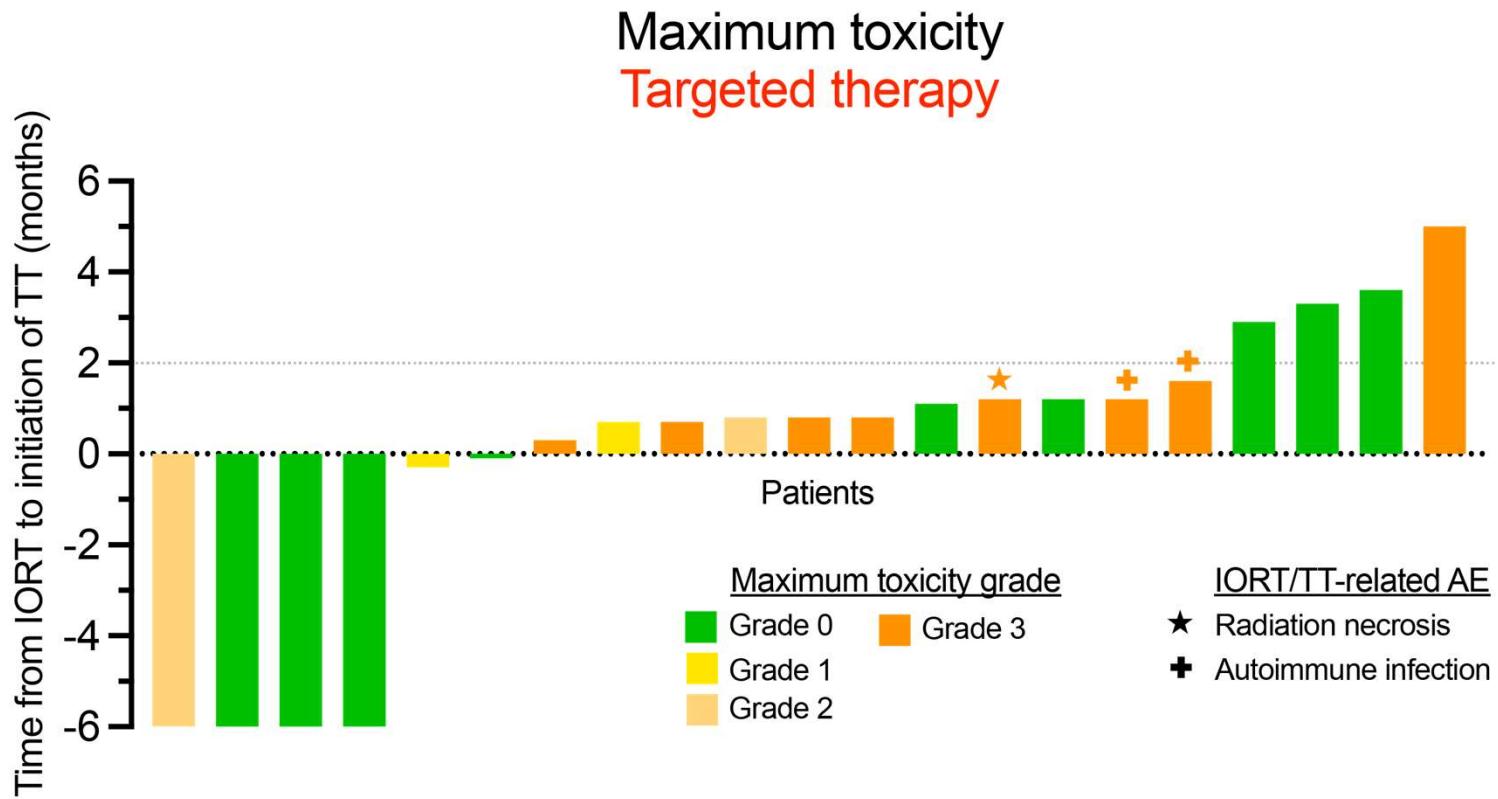
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# Safety

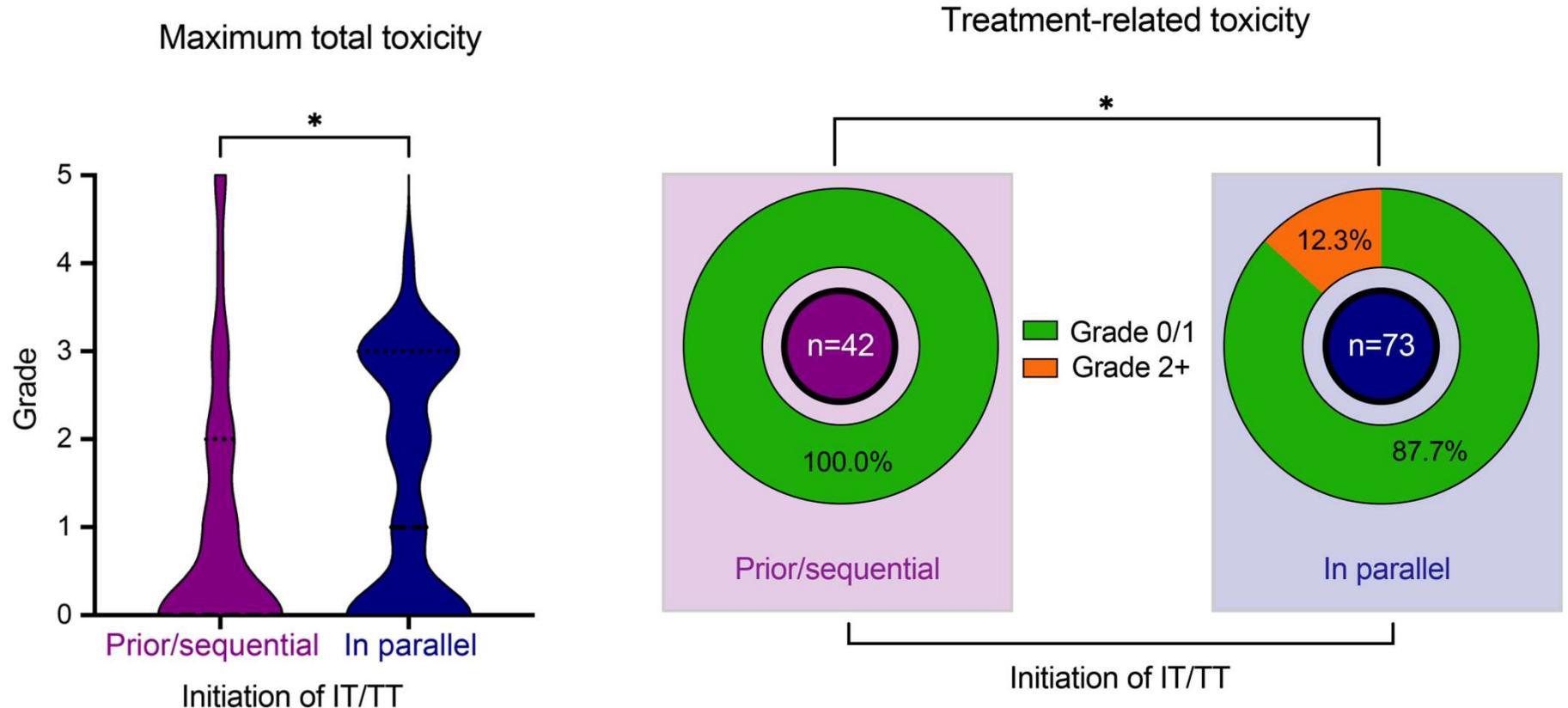
## Maximum toxicity Immune checkpoint inhibitor



# Safety

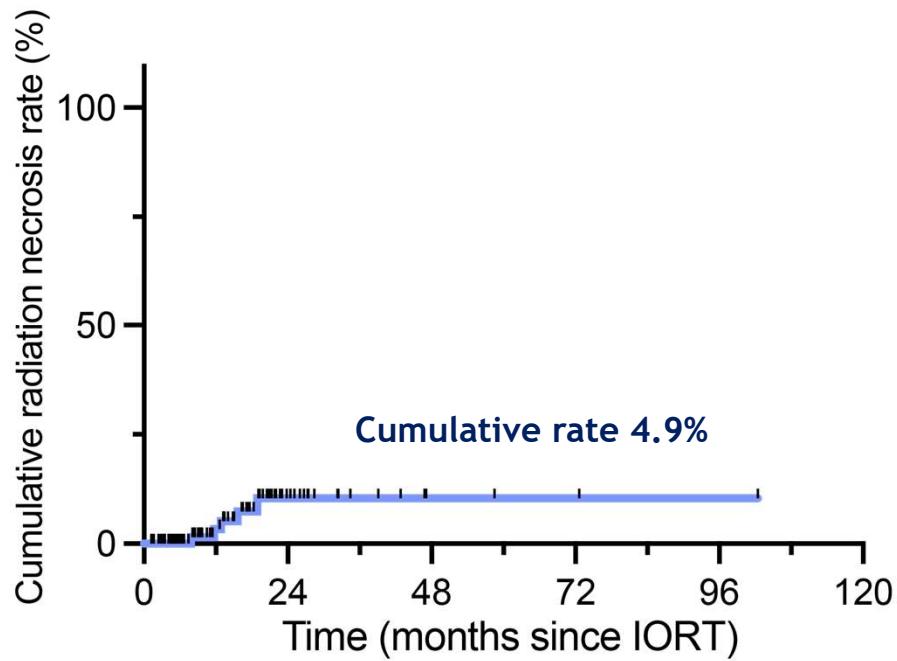


# Safety

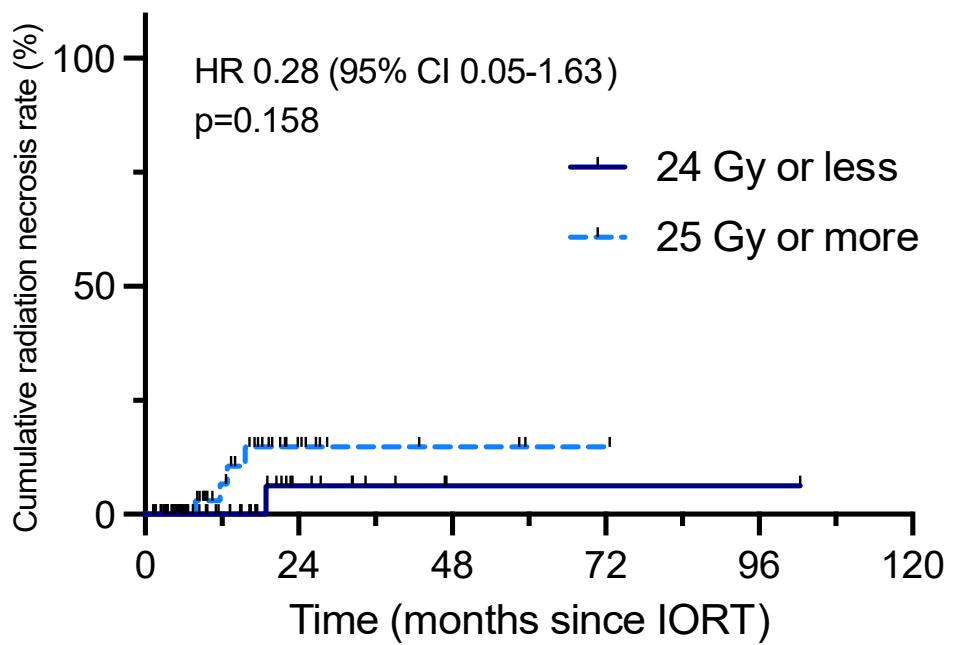


# Safety

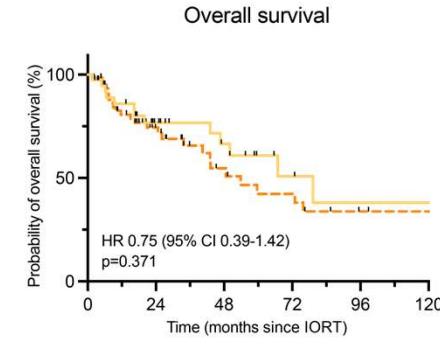
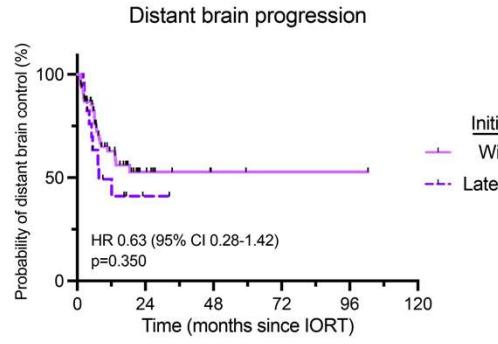
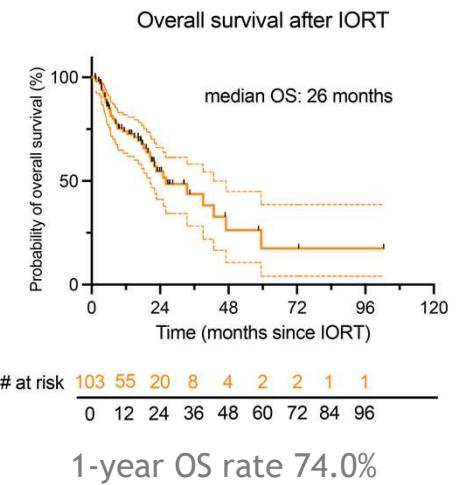
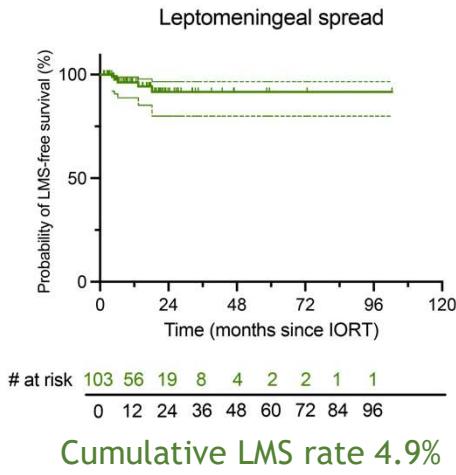
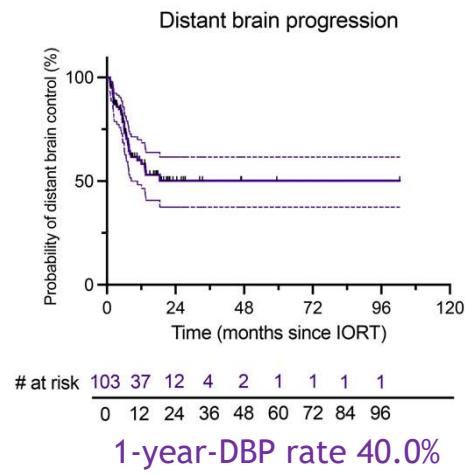
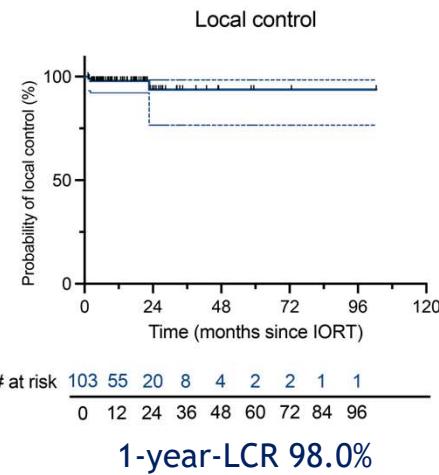
Radiation necrosis rate



Radiation necrosis



# Efficacy



# Conclusions

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IORT + TT / IT is safe

Encouraging local control for large metastases

Intervals between surgery and systemic treatment should be shortened

Prospective trials will elucidate true role of IORT

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## CLINICAL INVESTIGATION

### Multicentric Assessment of Safety and Efficacy of Combinatorial Adjuvant Brain Metastasis Treatment by Intraoperative Radiation Therapy and Immunotherapy



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Douglas Guedes de Castro, MD,<sup>¶</sup> Motaz Hamed, MD,<sup>#</sup> Cas S. Dejonckheere, MD,<sup>\*</sup> Daniel T. Cifarelli, MD,<sup>\*\*</sup>  
Lea L. Friker, MD,<sup>††</sup> Ulrich Herrlinger, MD,<sup>‡‡</sup> Michael Hözel, MD,<sup>†</sup> Hartmut Vatter, MD,<sup>#</sup> Matthias Schneider, MD,<sup>#</sup>  
Stephanie E. Combs, MD,<sup>||</sup> Leonard Christopher Schmeel, MD,<sup>\*</sup> Christopher P. Cifarelli, MD, PhD,<sup>\*\*</sup>  
Frank A. Giordano, MD,<sup>§§</sup> Gustavo R. Sarria, MD,<sup>\*</sup> and Klaus-Henning Kahl, MD,<sup>##</sup>

# Conclusions

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Multicentric registry

# Outlook



Multicentric registry

UNIVERSITÄTSKLINIKUM AUGSBURG

~ 100 pts



UUMM  
UNIVERSITÄTSMEDIZIN MANNHEIM

~ 50 pts

CHARITÉ  
UNIVERSITÄTSMEDIZIN BERLIN

total IORT pts:  
> 350 pts



Klinikum Stuttgart

~ 50 pts

ukb universitäts klinikum bonn

~ 100 pts

TUM

Technische Universität München

~ 50 pts

- +  
Potential further centers:
- Hamburg
  - Leipzig
  - Freiburg
  - Göttingen



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# Thank you very much for your attention.



Julian P. Layer  
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