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2-6 May 2025

Vienna, Austria

ESTRO HIGHLIGHTS: Neuro-Oncology

DR FADWA QACHACH

Joint ESTRO-EANO: **Recommandation on Reirradiation of glioblastoma**

Glioblastome

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Guidelines

ESTRO/EANO recommendation on reirradiation of glioblastoma

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Why a guideline for reRT of GB?

Parameter	Reported
OS	95%
Local control	75%
QoL	10%
Toxicity	95%
Follow-up	100%
Intervall	90%
Syst. Tx	70%

Parameter	Reported
Technique	100%
Imaging	70%
Registration	20%
PTV overlap	40%
Dose 1st RT	10%
Dose 2nd RT	100%
Dose sum 3D	15%

Parameter	Reported
OAR constraints	40%
Biol. Dose sum	25%
DHV PTV	35%
DVH OAR	25%
Cum DVH	10%

Level of reporting insufficient for quantitative analysis

REFERENCES: Systematic review data taken from Andratschke et al. Lancet Oncol 2022

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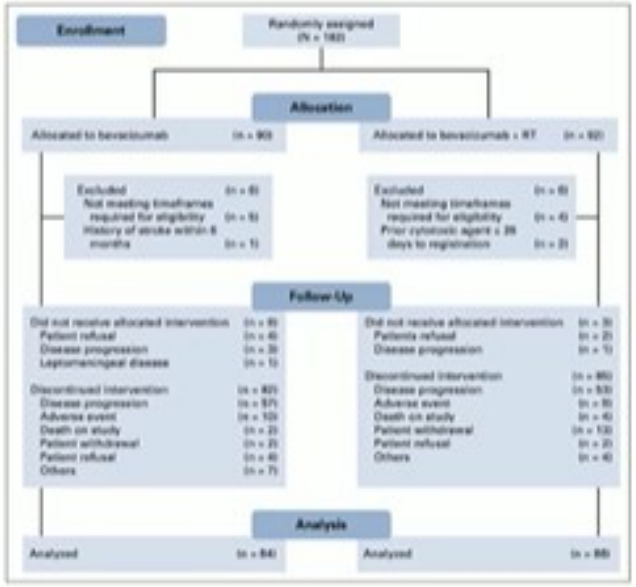
original reports

NRG Oncology/RTOG1205: A Randomized Phase II Trial of Concurrent Bevacizumab and Reirradiation Versus Bevacizumab Alone as Treatment for Recurrent Glioblastoma

Christina I. Tsien, MD[1]; Stephanie L. Pugh, PhD[2]; Adam P. Dicker, MD, PhD[3]; Jeffrey J. Raizer, MD[4]; Martha M. Matuszak, PhD[5]; Enrico C. Lallana, MD[6]; Joyl Huang, MD[7]; Ozer Algan, MD[8]; Nimisha Deb, MD[9]; Lorraine Portelance, MD[10]; John L. Villano, MS, PhD[11]; John T. Hamm, MD[12]; Kevin S. Oh, MD[13]; Arif N. Ali, MD[14]; Michelle M. Kim, MD[15]; Scott M. Lindhorst, MD[16]; and Minesh P. Mehta, MD[17]



- Clinical descriptors
- Relevant endpoints
- Toxicity and QoL
- Volumes of GTV / PTV

- Type of re-irradiation not defined
- No data on volume overlap
- No dosimetric data
- No cumulative OAR data

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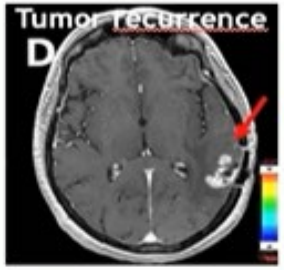
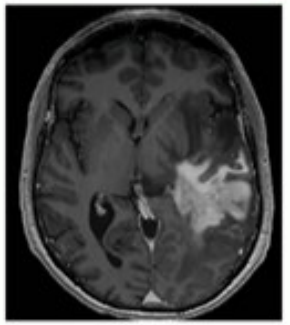
The ESTRO/EANO recomendation

Key questions based approach:

- KQ1: Which patients should be considered for reirradiation?
- KQ2: What imaging is required to assess recurrence after primary treatment of GB?
- KQ3: What are requirements for optimal target definition?
- KQ4: What is the recommended dose and fractionation for reirradiation?
- KQ5: What is the preferred treatment planning and delivery method?
- KQ6: How should cumulative doses be assessed with regards to safety?
- KQ7: What is the evidence for combined modality reirradiation?
- KQ8: What is the role of maintenance systemic therapy after reirradiation?
- KQ9: What follow-up schedule is recommended and what should be assessed?



A classical case



A non-classical case

How does it apply with 2 historic reirradiation cases?

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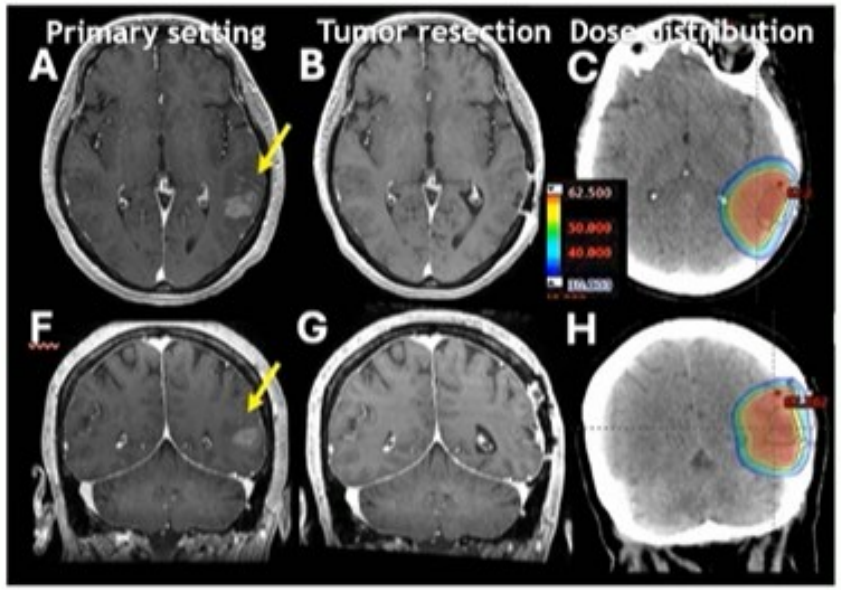
Case one: A classical approach

Primary treatment

- 48 year old female patient
- Glioblastoma MGMT methylated
- Initial symptoms: seizures
- Gross tumour resection
- Adjuvant radiotherapy 30 x 2 Gy with concurrent temozolomide
- 6 cycles adjuvant temozolomide



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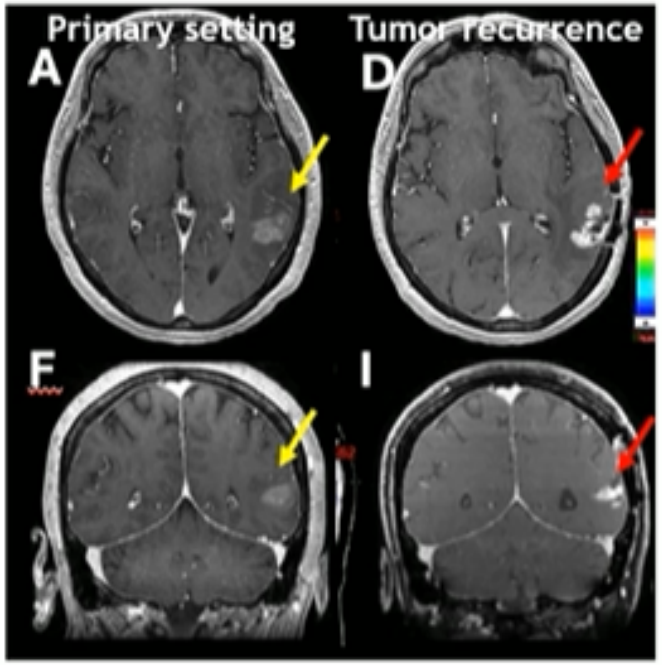
Case one: A classical approach

Tumor recurrence

- Two years later dysphasia as initial symptoms
- cMRI revealed suspicion of recurrent tumor
- Reirradiation Type 1
- Multidisciplinary tumorboard: Recommendation of reirradiation



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KQ1:

Which patients should be considered for reirradiation?

Recommendations / Statements	Strength	Level of evidence
Reirradiation of patients with recurrent glioblastoma should be based on **individual decision making** and should only be recommended after careful **discussion in an MDT** balancing risks, benefits, and treatment alternatives	Strong	Expert opinion
Reirradiation of patients with recurrent glioblastoma may be considered with a **KPS >=60** and an **interval >6 months** from the previous radiotherapy ndependent of age or MGMT methylation status	Conditional	Moderate
After gross total resection of recurrent glioblastoma reirradiation may be considered in patients with favorable prognostic factors	Conditional	Low
Although reirradiation has not yet been shown to provide an OS benefit, a prolongation of progression-free survival can be expected after careful patient selection		Moderate

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KQ2:

What imaging is required to assess recurrence after primary treatment of GB?

Recommendations / Statements	Strength	Level of evidence
To assess recurrence, particularly in-field, **contrast-enhanced T1-weighted imaging** is required, and the addition of **advanced MRI or AA-PET** is recommended for ist differentiation from pseudoprogression/ radiation necrosis	Strong	Low
Advanced imaging techniques (i.e., perfusion MRI, MR spectroscopy, AA-PET) increase diagnostic accuracy for **differentiation of recurrence from pseudoprogression**, but no technique, nor combination of techniques, is clearly superior to the other.	---	Low

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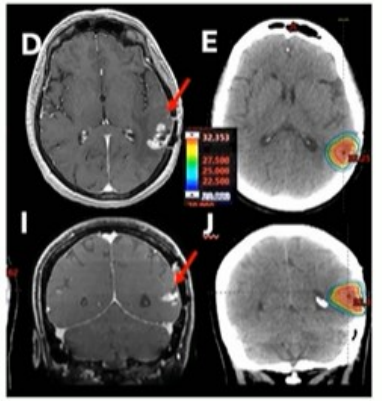
Tumor recurrence:

- Recommendation for a second course of radiation
- Target volume definition:
  - T1-weighted MRI
  - PTV= GTV + 3 mm



KQ3:

What are requirements for optimal target definition?

Recommendations / Statements	Strength	Level of evidence
Rigid image registration for target volume definition and dose accumulation is recommended.	Strong	Moderate
T1-weighted contrast enhancing lesions, new or progressive **T2/FLAIR** abnormalities, and **AA-PET**-avid regions should be included in the GTV.	Strong	Expert opinion
A **CTV margin is not mandatory**, but a GTV to CTV margin of 3-5 mm can be added optionally (depending on overall volume, dose/fractionation and pattern of recurrence), while a **maximum CTV to PTV of 3mm** is recommended.	Strong	Expert opinion
If functional imaging is considered, both **AA-PET** as well as **multiparametric MRI** are valid options, although no consensus could be reached to whether or not to include perfusion suspect regions into the GTV.	Strong	Expert opinion

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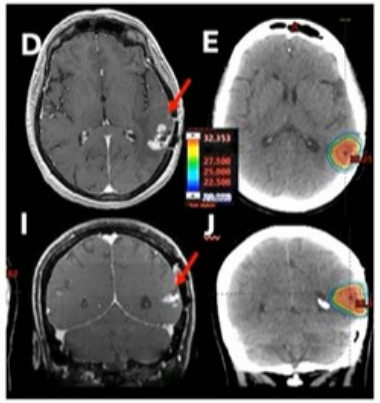
Tumor recurrence:

- Recommendation for a second course of radiation
- Treatment: 5x5.5 Gy



KQ4:
What is the recommended dose and fractionation for re-irradiation

Recommendations / Statements	Strength	Level of evidence
A treatment in which a sufficient dose is delivered is preferred, and therefore, the biological effective dose should be above 36 Gy in 2 Gy fractions.	---	Moderate
Hypofractionated radiosurgery is preferred for lesions (GTV size) ≤ 3cm.	Strong	Expert opinion
There is no upper threshold volume for (hypo-) fractionated IGRT of lesions > 3cm.	Conditional	Expert opinion

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KQ7/ 8:
What is the evidence for combined modality re-irradiation? What is the role of maintenance systemic therapy after re-irradiation?

Recommendations / Statements	Strength	Level of evidence
For combined modality treatment **target definition, dose and fractionation should not be adjusted**.	Strong	Expert opinion
The use of systemic treatment together with re-irradiation of recurrent glioblastoma should be further explored in prospective clinical trials.	Strong	Expert opinion
Combined modality treatment in re-irradiation appears to be well tolerated but has **not been shown to provide an OS benefit**.	---	High
A clear recommendation for this approach, especially with respect to a specific drug combination, cannot be given.	---	Moderate
Currently, there is **no indication for adjuvant systemic therapy** after re-irradiation.	---	Expert opinion

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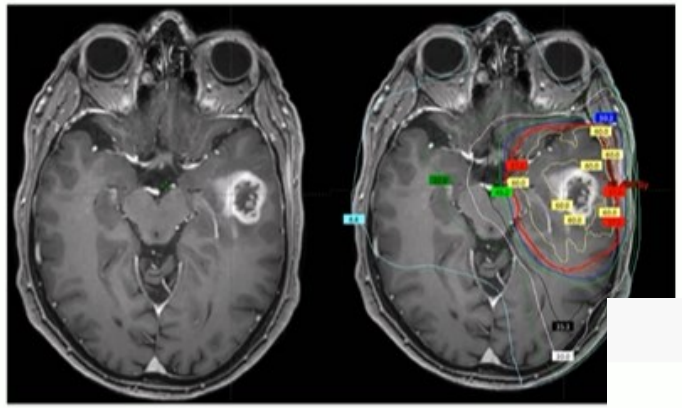
Case two: A non- classical approach

Primary treatment

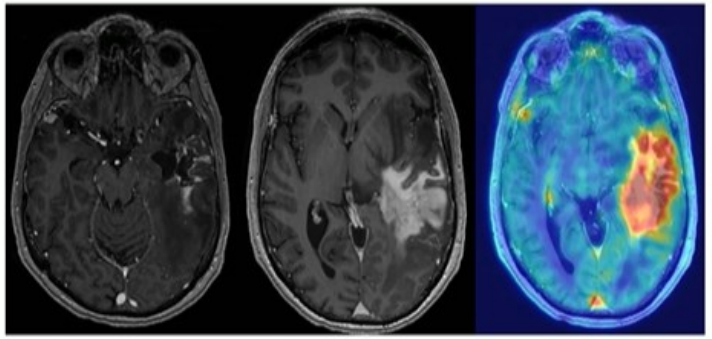
- 57 year old male patient
- Glioblastoma MGMT methylated
- Initial symptoms: seizures
- Gross tumour resection
- Adjuvant radiotherapy 30 x 2 Gy with concurrent temozolomide
- 6 cycles adjuvant temozolomide



Case two: A non- classical approach

Tumor recurrence / persistence

- 2 cycles temozolomide
- 11 cycles Bevacizumab
- 2 cycles lomustine
- 8 cycles Bevazizumab



➔ 4x switch of systemic therapy due to progression **over 33 months**.

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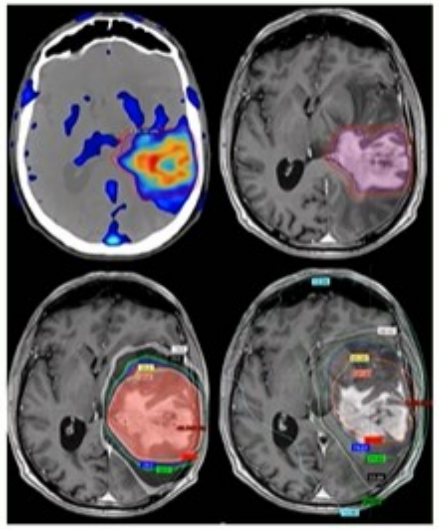
Tumor recurrence:

- Recommendation for a second course of radiation

- GTV: CE T1 weighted images + FET-avid regions
- No CTV
- PTV: +3 mm

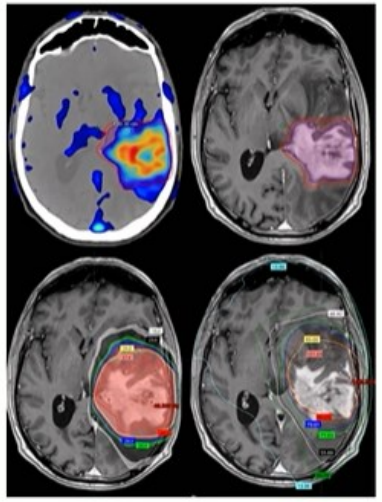


Tumor recurrence: Treatment

- Prescribed dose:
  10 x 3.5 Gy homogenous
- max. GTV diameter: 8 cm
- GTV: 81.6 cc, PTV: 130.1 cc

Cumulative doses (EQD2)

- Dmean (brain) = 26.8 Gy
- D0.1cc (brain) = 108.16 Gy
- D0.1cc (brainstem) = 77.09 Gy
- Optic structures respected



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KQ5:
What is the preferred treatment planning and delivery method?

Recommendations / Statements	Strength	Level of evidence
Advanced IGRT techniques should be employed for high dose re-irradiation	Strong	low
EQD2Gy dose recalculation is preferred (over BED and EUD) and should be used for dose accumulation, as it is most commonly used in the literature and easy to interpret.	Strong	moderate
The minimum set of OAR to evaluate after biological dose accumulation include: **brain, brain stem, chiasm, optic nerves/ tract, cranial nerves** in close proximity to PTV	Strong	Expert opinion

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KQ6:
How should cumulative doses be assessed with regards to safety?

Recommendations / Statements	Strength	Level of evidence
PTV prescription and compromise should follow the following cascading steps: 1) No PTV compromise if cum. OAR doses are deemed safe and/ or acceptable. 2) **PTV compromise** allowed to keep cumulative OAR doses safe and/ or acceptable. 3) If a reasonable CTV / GTV dose coverage is not to be achieved, **dose prescription may be adapted** to reach safe or acceptable OAR doses.	Strong	Expert opinion
Recovery from previous irradiation has only consistently been described for brain tissue and spinal cord and thus, should only be considered for assessing cumulative doses in these organs	Strong	Low

FET-PET and SRS in Recurrent Glioblastoma

FET-PET and SRS in Recurrent Glioblastoma

Tumor treating fields (TTFields) and Stereotactic Radiosurgery Guided by FET-PET for **rGBM** (TTaRGET)

A Phase 2, Single-arm, Externally-Controlled Trial

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im. Jana i Jędrzeja Śniadeckich

ESTRO 2025 2-6 May 2025 Vienna, Austria

CENTRUM ONKOLOGII
im. prof. F. Łukaszczyka w Bydgoszczy

FET-PET and SRS in Recurrent Glioblastoma

Background

- Efficacy of stereotactic radiosurgery in recurrent glioblastoma (**rGBM**) is limited due to **extensive invasion that is poorly visible on MRI**.
- FET-PET (18F-fluoro-ethyl-tyrosine-PET) **refines target volumes** and decreases geografical misses[1,2,3,4]
- **Tumor Treating Fields (TTFields)** , a non-invasive approach that uses low-intensity alternating electric fields to disrupt tumor cell division, are approved in rGBM based on **EF-11 trial (SoC vs TTFields montherapy – a multicenter randomized trial).**
- In rGBM median OS ranges **from 3-9 months** and **1-year OS rate 20-44%** underscoring the need for more effective combination strategies.

[1]Munck Af Rosenschold et al. [2]Anca-L Grosu et al. [3]Aimee R Hayes et al. [4]Maximilian Niyazi et al.

FET-PET and SRS in Recurrent Glioblastoma

Hypothesis and Aims

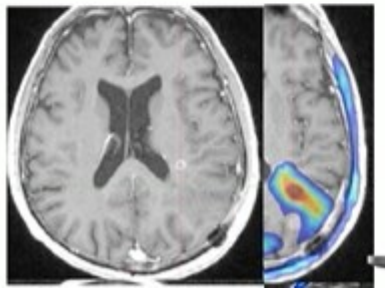
- **Hypothesis:** Biologically-defined targets for SRS combined with TTFields will be complementary and improve outcomes with minimal toxicity
- **Aim:** To study the efficacy and safety of FET-PET-based SRS in combination with TTFields

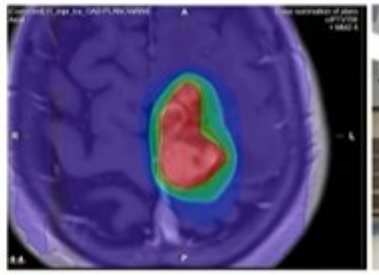
FET-PET and SRS in Recurrent Glioblastoma

Methods

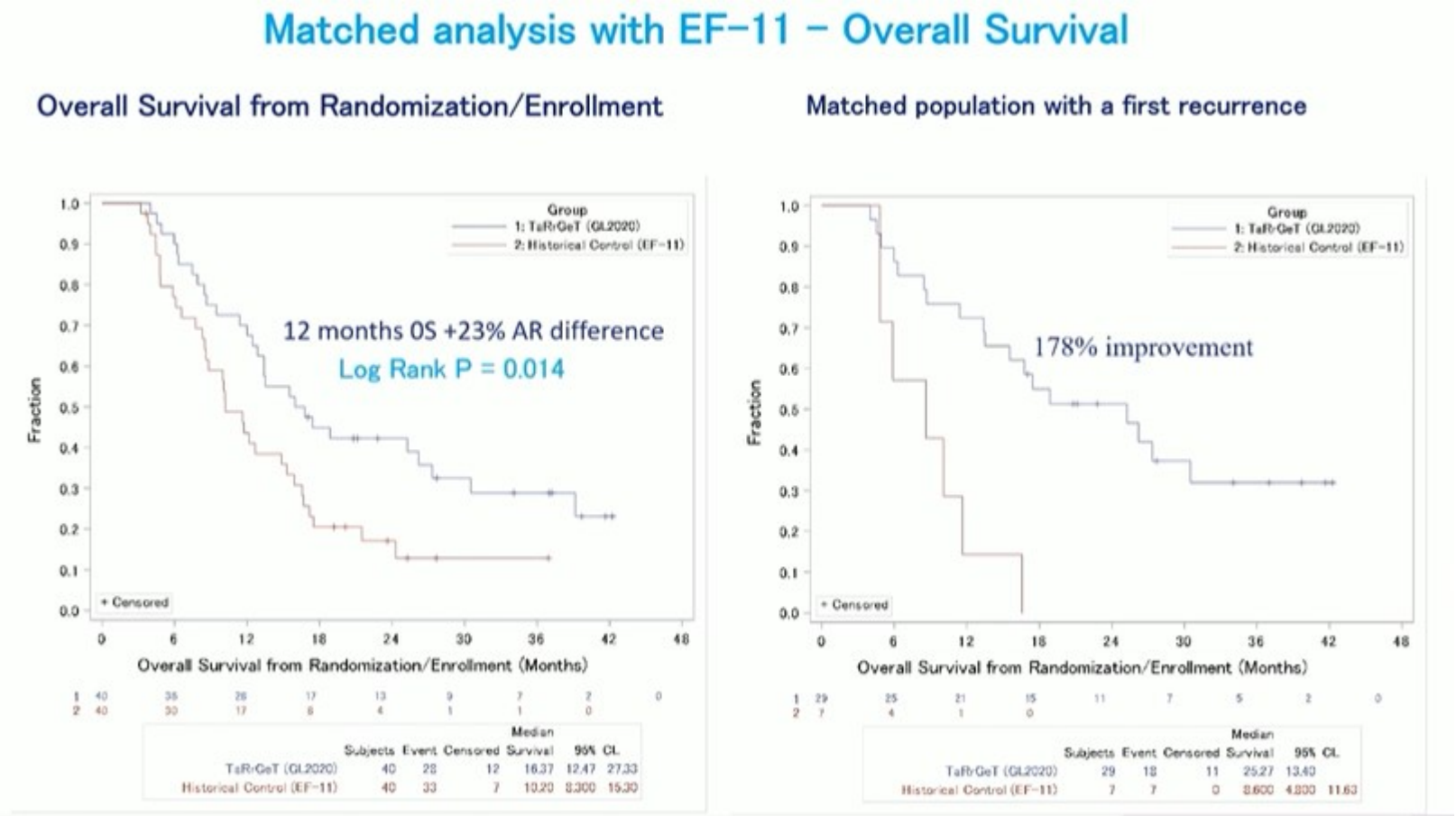
- 40 patients with recurrent glioblastoma according to WHO 2016 classification (NCT04671459)
- FET-PET/MRI hybrid scanner for SRS treatment planning – dual FET-PET aquisition
- TTFields started within 7 days of FET-PET
- SRS/mf-SRS (1 x 18-20 Gy or 5 x 5-6 Gy) within 14 days of FET-PET
- Preplanned comparison with EF-11 trial (TTFields monotherapy for rGBM vs SoC):
  - +20% increase in 1-year survival rate needed to find significant difference
  - Same inclusion and exclusion criteria
  - Propensity score matched analysis

FET-PET → 7 days → TTFields → 7 days → SRS

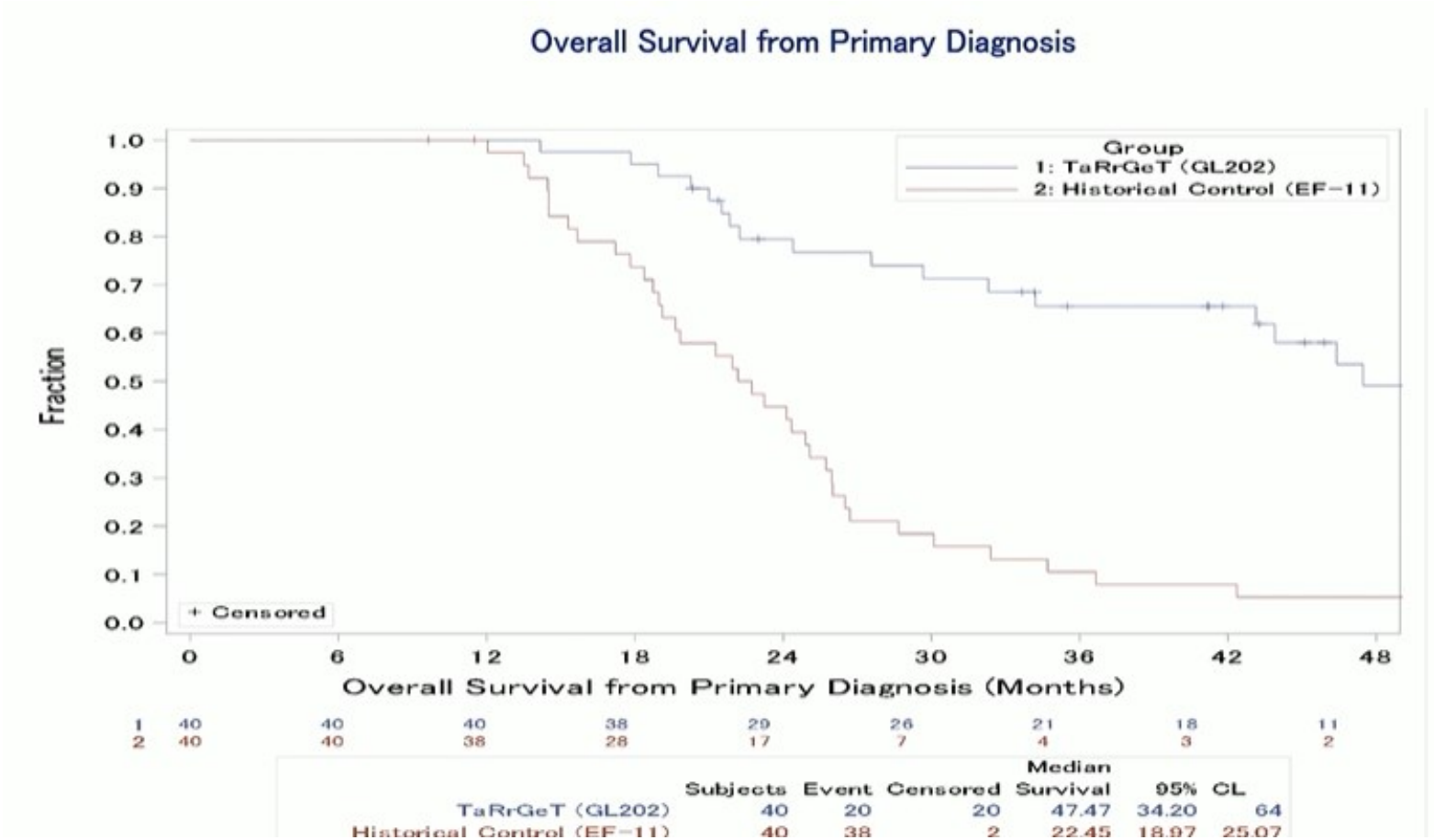


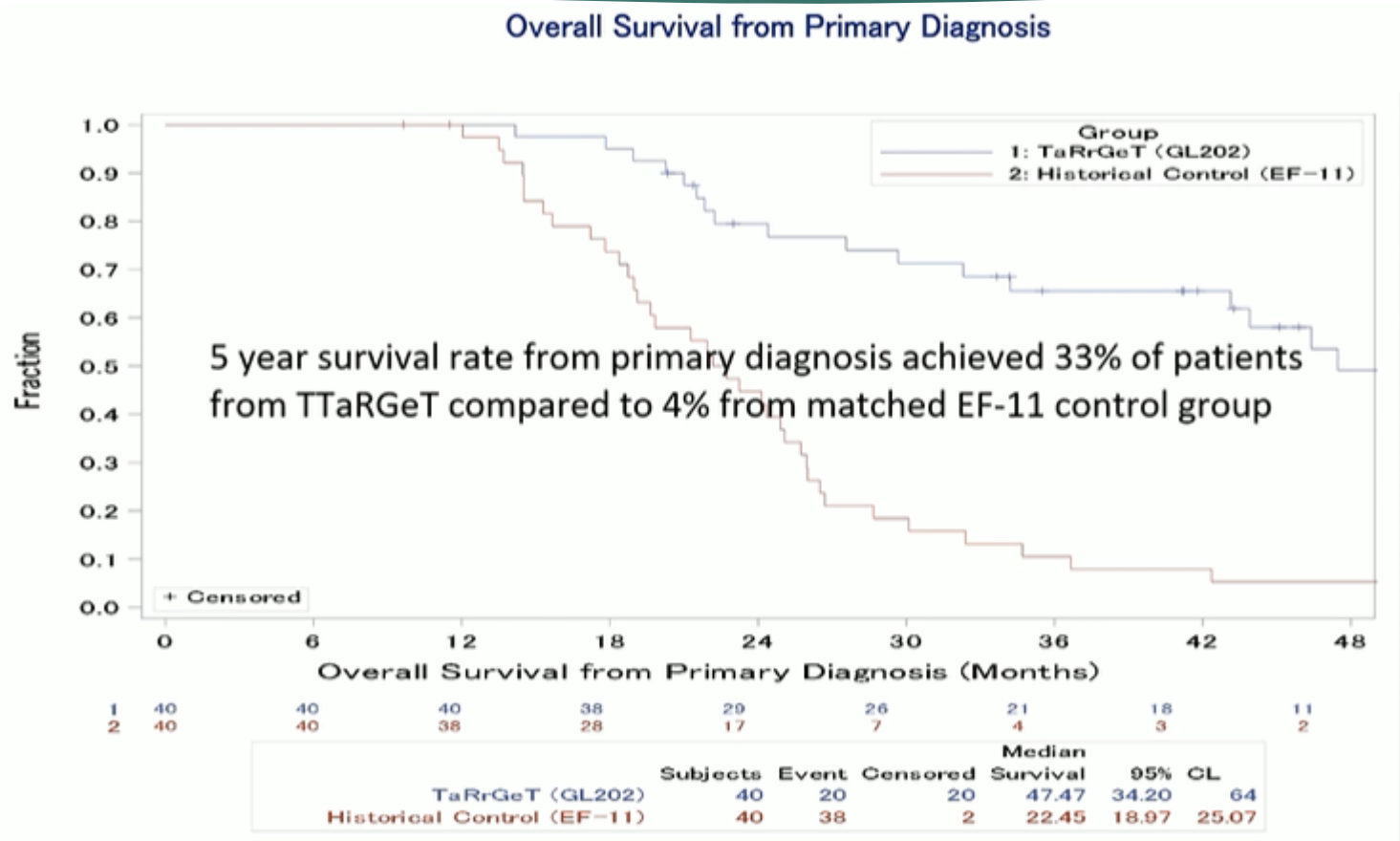

FET-PET and SRS in Recurrent Glioblastoma



FET-PET and SRS in Recurrent Glioblastoma



FET-PET and SRS in Recurrent Glioblastoma



FET-PET and SRS in Recurrent Glioblastoma

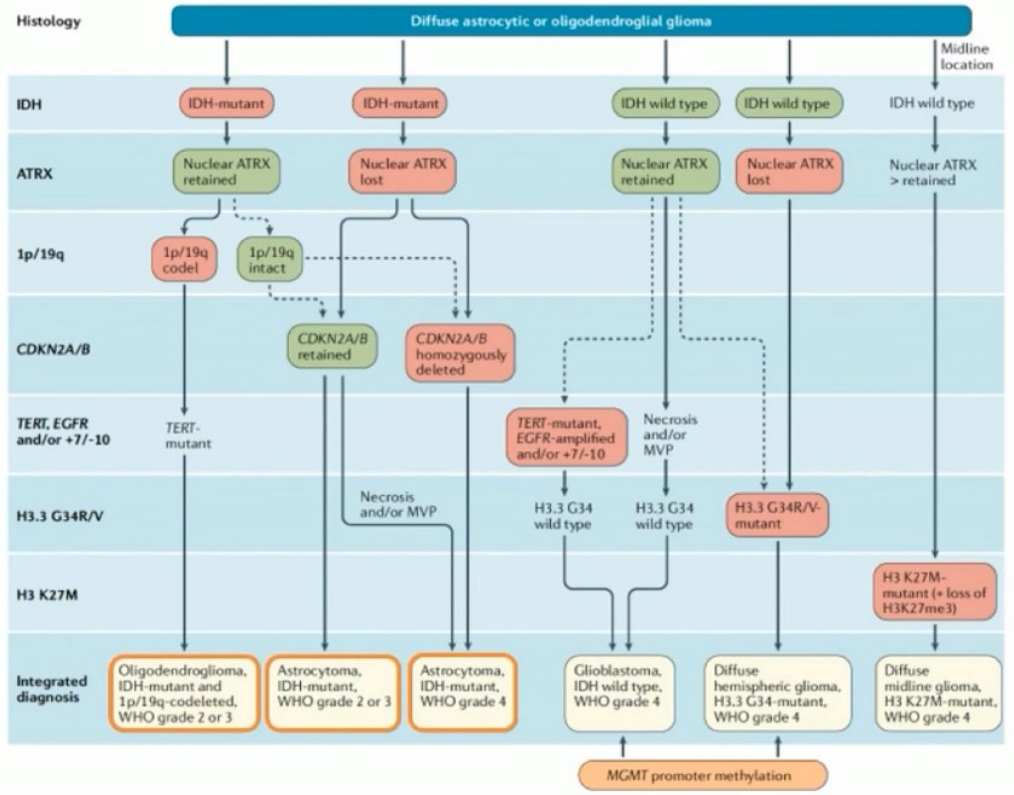
Conclusions

- TTaRGET is more effective than pre-defined before the trial (+23% improvement in annual survival rates -PSM)
- TTaRGET is effective in MGMT methylated and unmethylated subgroups
- TTaRGET is safe and well tolerated, although RICE remains a frequent complication (mainly asymptomatic)

Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

Diagnosis



MVP, microvascular proliferation.
Weller M, et al. Nat Rev Clin Oncol. 2021;18:170-186.

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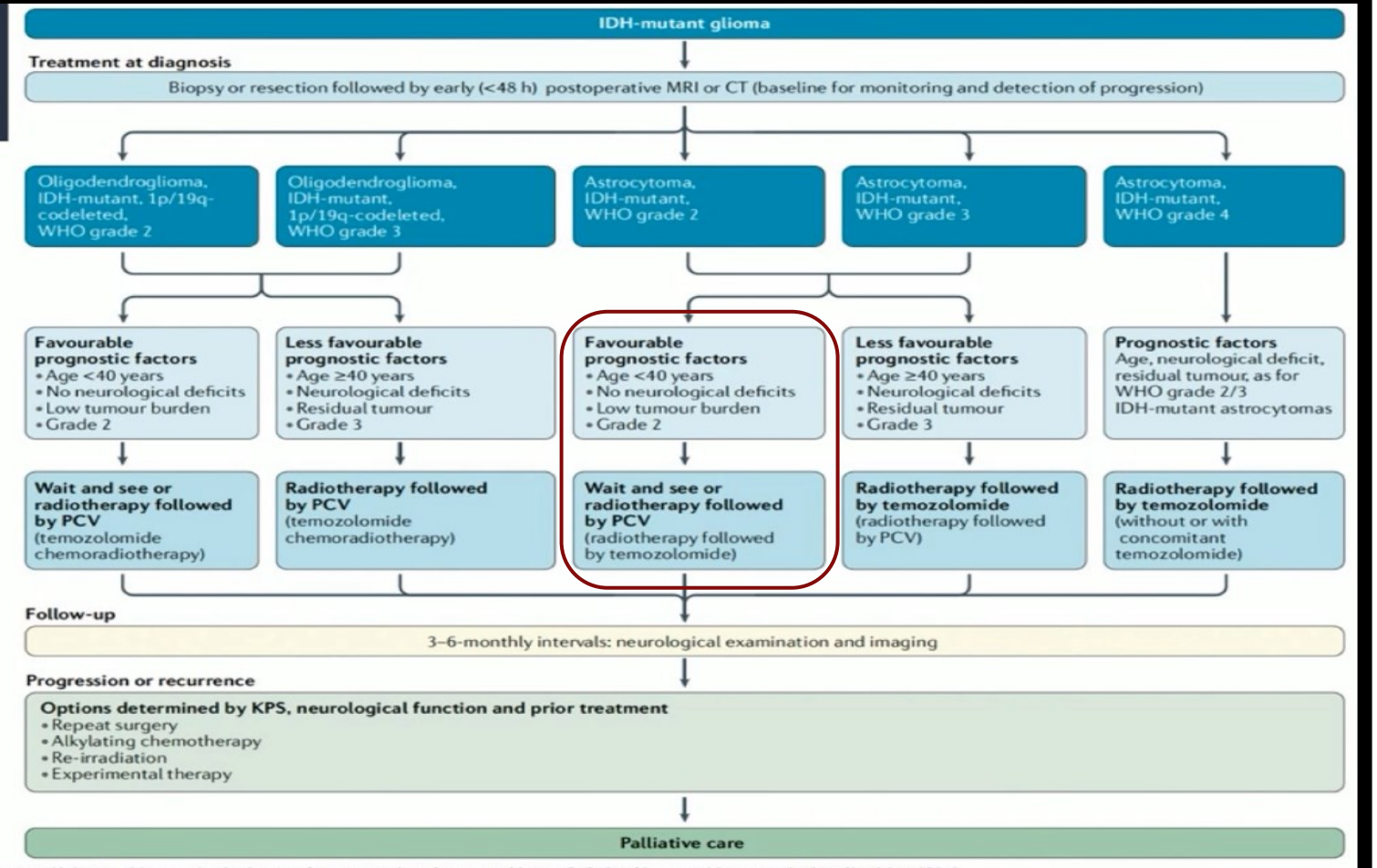
Therapy



CT, computed tomography;
KPS, Karnofsky Performance Scale.
Weller M, et al. Nat Rev Clin Oncol. 2021;18:170-186.

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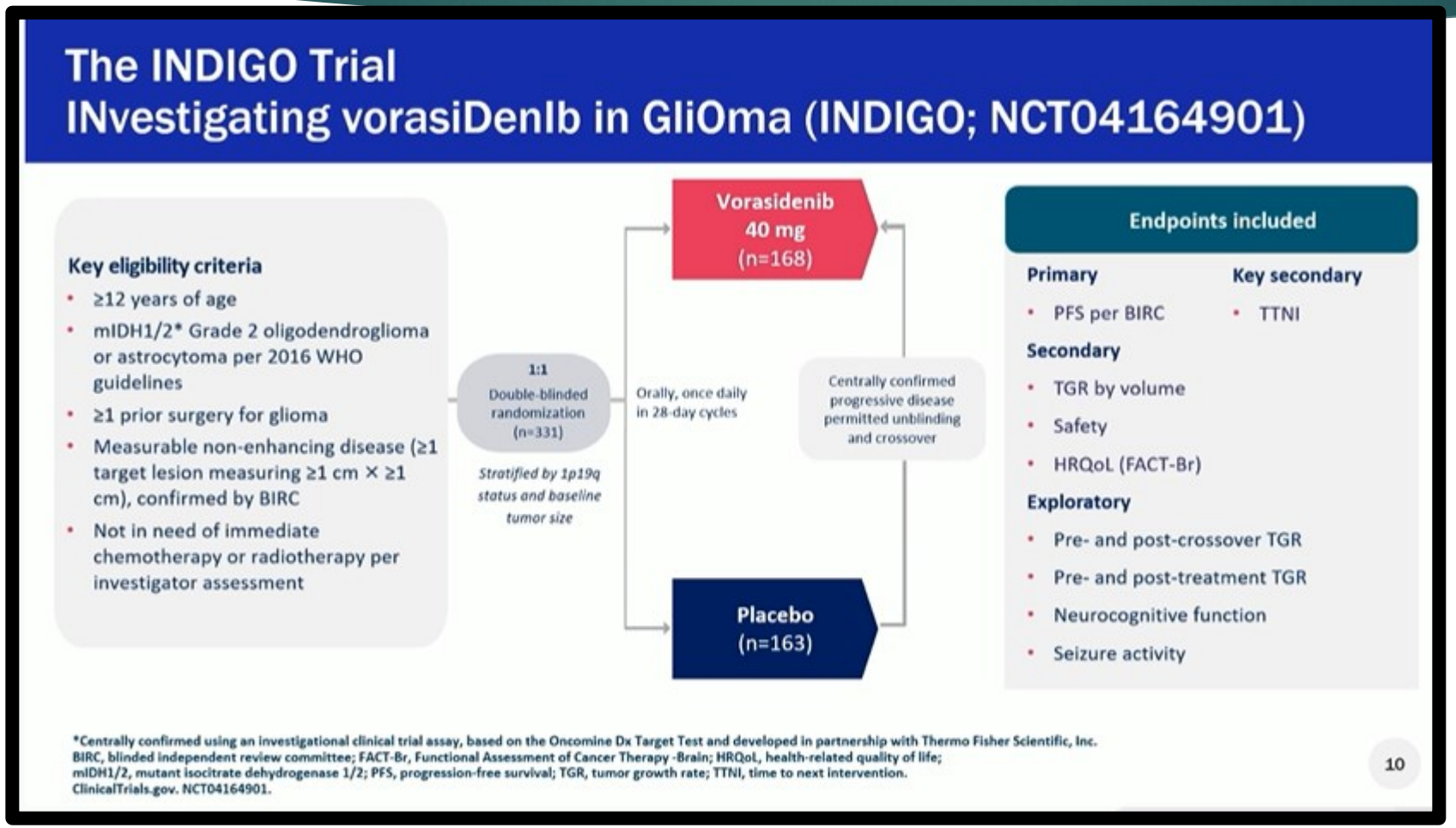


Emergence des IDH Inhibitors.

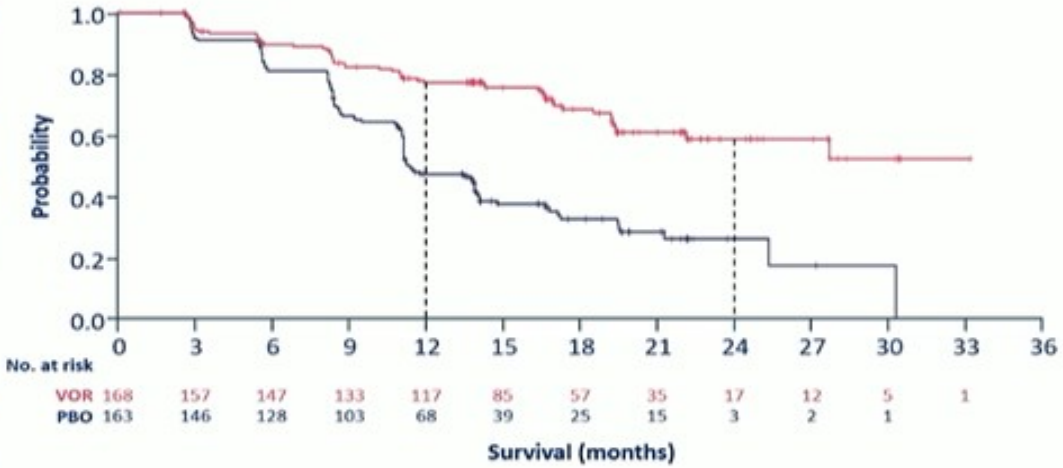
Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

ASCO, The American Society of Clinical Oncology; IA2, second interim analysis; PFS, progression-free survival; SNO, The Society for Neuro-Oncology; TTNI, time to next intervention.
1. Mellinghoff IK, et al. *N Engl J Med*. 2023;389(7):589–601; 2. Mellinghoff IK, et al. *J Clin Oncol*. 2023;41(Suppl.17):LBA1.

Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

Primary Endpoint: PFS per BIRC

	Vorasidenib (n=168)	Placebo (n=163)
Events – n (%)	54 (32.1)	104 (63.8)
Median (95% CI)	**NE (22.1, NE)**	**11.4 (11.1,13.9)**
HR (95% CI)	Mar 7, 2023: 0.35 (0.25, 0.49) *[Sep 6, 2022: 0.39 (0.27, 0.56)]*[1]	
P value	0.00000000013*	



12 months:
Vorasidenib: 77.3%
Placebo: 47.3%

24 months:
Vorasidenib: 58.8%
Placebo: 26.2%

*This P value cannot be used to claim statistical significance.
PFS was the time from randomization up to death or radiographic progressive disease and was assessed by the BIRC per modified RANO-LGG.
PFS per investigator results were consistent with these findings, with an HR of 0.34 (95% CI 0.23–0.50). Data cut-off: March 7, 2023.
BIRC, blinded independent review committee; NE, not evaluable; PBO, placebo; RANO-LGG, Response Assessment in Neuro-Oncology-low-grade glioma; VOR, vorasidenib.
Mellinghoff IK et al. *J Clin Oncol 2023*;41(Suppl.17):LBA1.

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Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

Vorasidenib has a Manageable Safety Profile[1,2]

	Vorasidenib (N=167)	Placebo (N=163)
Any Grade ≥3 AE – n (%)	38 (22.8)	22 (13.5)
Increased alanine aminotransferase	16 (9.6)	0
Seizure	7 (4.2)	4 (2.5)
Increased aspartate aminotransferase	7 (4.2)	0
Increased gamma-glutamyltransferase	5 (3.0)	2 (1.2)
Syncope	3 (1.8)	1 (0.6)
Hypertension	2 (1.2)	3 (1.8)
Decreased neutrophil count	2 (1.2)	0

Treatment interruption due to TEAE
- **Vorasidenib** 29.9% (n=50)
- **Placebo** 22.7% (n=37)

Dose reduction due to TEAE
- **Vorasidenib** 10.8% (n=18)
- **Placebo** 3.1% (n=5)

Discontinuation due to TEAE
- **Vorasidenib** 3.6% (n=6)
- **Placebo** 1.2% (n=2)

No fatal TEAE

The safety set included all the patients who received at least one dose of study treatment. Preferred terms listed are those that occurred at Grade ≥3 in 2 or more patients in the vorasidenib group.

AE, adverse event; TEAE, treatment-emergent adverse event.

1. Mellinghoff IK, et al. *N Engl J Med*. 2023;389(7):589-601.
2. Servier Pharmaceuticals – Data on File

Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

New Results Generate Many New Questions

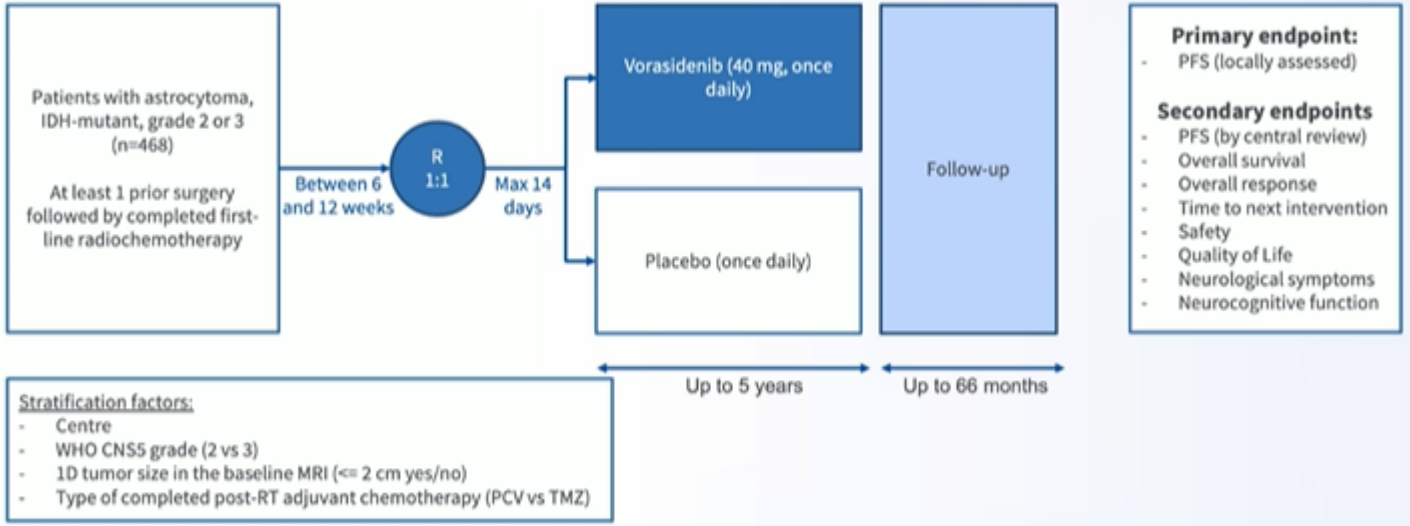
- Vorasidenib for which patient and when?
- OS benefit of vorasidenib?
- How to improve accuracy of tumor grading?
- Vorasidenib and/or radiochemotherapy in first line?
- Vorasidenib at progression after radiochemotherapy?
- Vorasidenib for Grade 3 and 4 IDH-mutant gliomas?
- Molecular biomarkers for response?
- Vorasidenib for contrast-enhancing gliomas?
- Advanced neuroimaging and PET for patient selection and follow-up?
- Sequencing or combining vorasidenib with other targeted therapies?
- Vorasidenib as maintenance treatment?

IDH, isocitrate dehydrogenase; OS, overall survival; PET, positron emission tomography.

Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse glioma**

Phase III trial EORTC-2427 (VIGOR)

PI: M. Preusser, Co-PI: M. Geurts



EORTC European Organisation for Research and Treatment of Cancer

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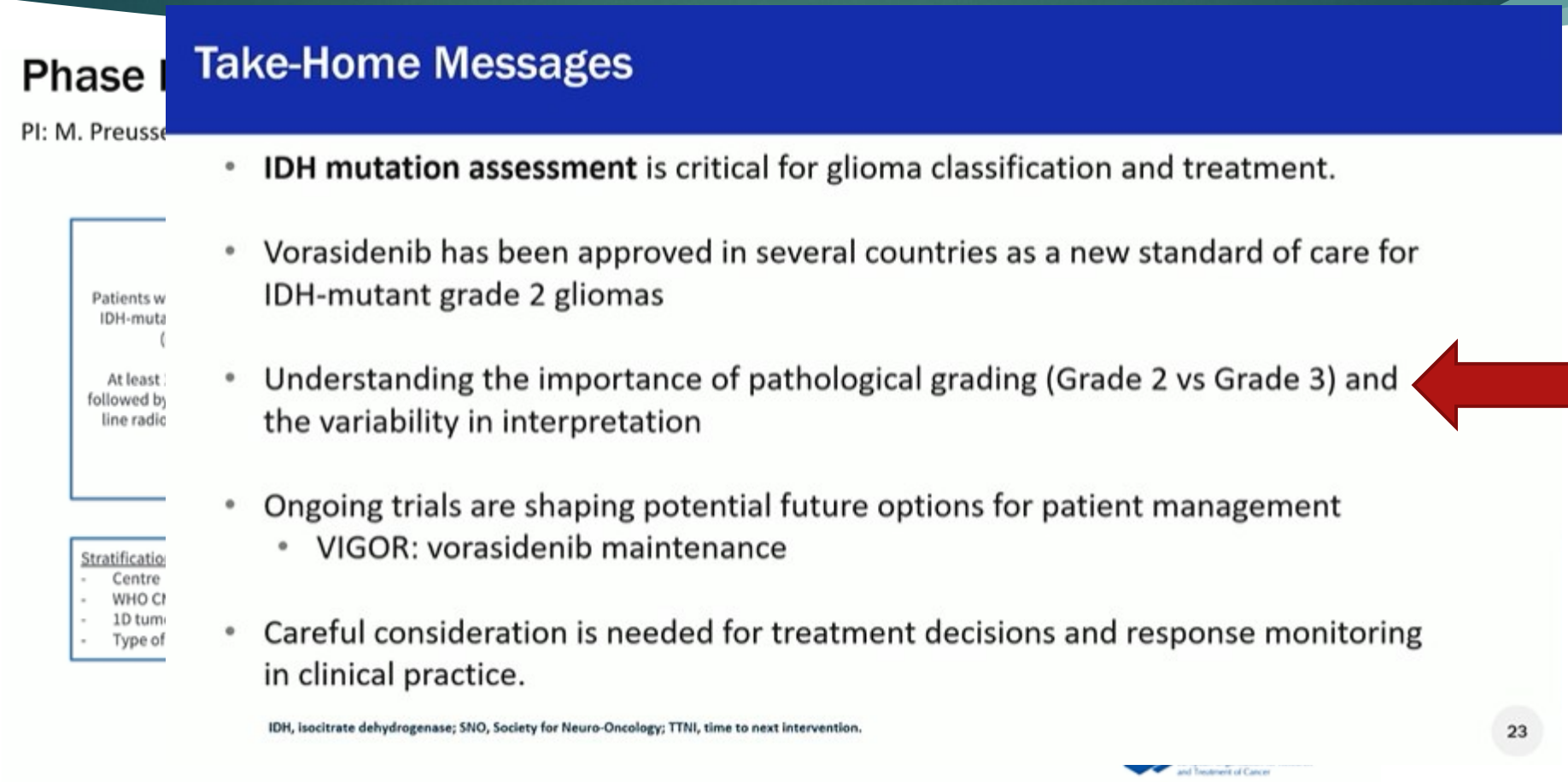
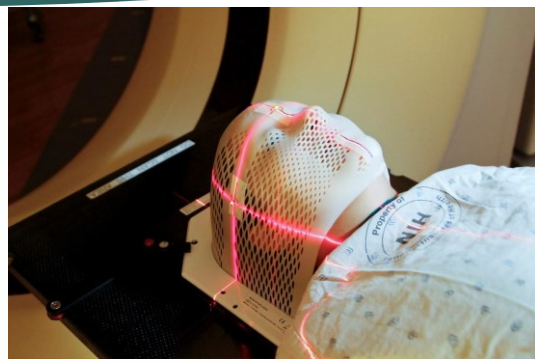


Plus de précision par l'anapath

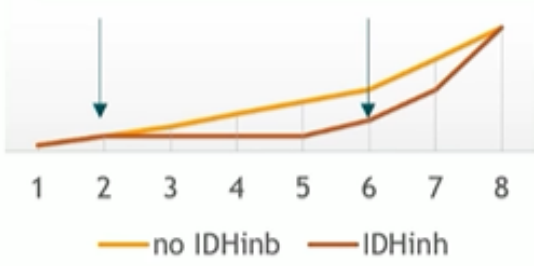
Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

WHEN: In era of IDH inhibitors - when to use RT

- Those not eligible for IDH inhibitors (off trials)
  - **Grade 4 - post op**
  - **Grade 3 - post op (or if foci G3 progressing)**
  - **Grade 2 - progressing tumour or poor prognostic features**
    - Unable to have drug (e.g. deranged LFTs)
    - Do not want IDH inhibitor
    - Grade 2 on biopsy but marked enhancement (probably not grade 2)
- Those coming off IDH inhibitor
  - Adverse effects (e.g. raised transaminases +++)
  - Progressive disease
    - Now no longer dependent on 2HG- is it the same disease??
    - Will they grow faster? NO data yet but theoretically
    - Importance of getting pre and post-IDHinhib samples compared



What if biology changes - we don't know yet



Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

HOW - PLANNING - ESTRO EANO recommendations

TARGET DELINEATION


Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

ESTRO-EANO guideline on target delineation and radiotherapy for IDH-mutant WHO CNS grade 2 and 3 diffuse glioma

Brigitta G. Baumert, Jaap P. M. Jaspers, Vera C. Keil, Norbert Galldiks, Ewa Izycka-Swieszewska, Beate Timmermann, Anca L. Grosu, Giuseppe Minniti, Umberto Ricardi, Frédéric Dhermain, Damien C. Weber, Martin van den Bent, Roberta Rudà, Maximilian Niyazi, Sara Erridge

- Fused MRI -
  - Preferably 3 Tesla
  - 3D T1 pre and post contrast and 3D FLAIR
  - Low grade glioma ideally 3-4 months post op to allow surgical changes to settle
  - High grade glioma - new MRI for planning (but post op oedema may not have settled)

- PET: less evidence than for IDH wildtype glioma and not widely available - area of ongoing research

- OARs - standard 'brain set'
  - Tolerances - same as for IDH wild-type (see ESTRO IDH wildtype guidelines)
  - Greater importance of trying to reduce long term neuro-cognitive effects
    - sparing normal brain (e.g. keep mean brain-GTV as low as possible)
    - hippocampi (esp contralateral) (e.g. keep D40% bilateral hippo to <7.3Gy)

Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

HOW - PLANNING - ESTRO EANO IDH mutated recommendations

MARGINS:

	GRADE 2	GRADE 3	GRADE 4
GTV	Resection cavity and any residual tumour after surgery PET or perfusion /diffusion MRI may help distinguish oedema and tumour		
	T2/FLAIR almost certainly tumour	T2/FLAIR could be either tumour or oedema	T2/FLAIR could be either tumour or oedema
CTV	10mm expansion -edited	15mm expansion -edited	15mm expansion -edited
PTV	Departmental specific - usually ≤ 3mm		

Joint ESTRO-EANO: Advances in the treatment of **adult-diffuse gliomas**

HOW: ESTRO EANO IDH mutated recommendations: DOSE

Trials investigating radiotherapy dose and timing in grade 2 and 3 diffuse glioma.

Trial name	Inclusion	Astro		Oligo		"Oligo astro"		Randomisation	Radiotherapy	Conclusions
		2	3	2	3	2	3			
Early vs late										
EORTC 22,845 [38]	1986–1997	x		x		x		RT vs observation	28*1.8 Gy	No OS benefit (7.4 vs 7.2y) but PFS benefit (5.3 vs 3.4y) for early RT
Alliance N0577 (CODEL) [86]	2009–2011				x			RT vs RT + TMZ vs TMZ	33*1.8 Gy	PFS worse in TMZ only arm (5y PFS 56 % vs 33 %). Study design changed to RT + PCV vs RT + TMZ
EORTC 22,033 [47]	2005–2010	x						RT vs TMZ	28*1.8 Gy	No difference in PFS (3.8 vs 3.3y)
Dose escalation										
EORTC22844 [44]	1985–1991	x		x		x		RT vs dose-escalated RT	25*1.8 Gy vs 33*1.8 Gy	No OS benefit (5y OS 58 % vs 59 %) or PFS benefit (5y PFS 47 % vs 50 %) for high dose RT
Intergroup [73]	1986–1994	x		x		x		RT vs dose-escalated RT	28*1.8 Gy vs 36*1.8 Gy	No OS benefit (15y OS 22 % vs 25 %) or PFS benefit (15y PFS 15 % vs 10 %) for high dose RT

	Grade 2		Grade 3		Grade 4
	50.4Gy 28 fractions		59.4Gy 33 fractions		60Gy 30 fractions
Alternative	54Gy 30 fractions				59.4Gy 33 fractions
	codel	non-codel	codel	non-codel	
Adj Chemo	PCV x 6	PCV x 6 or TMZ x12	PCV x 6	TMZ x 12	TMZ x 6

Neoadjuvant SRS for Brain Metastases

Neoadjuvant SRS for Brain Metastases

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INTERnational collaboration of NEOadjuvant stereotactic radiosurgery for brain metastases: the INTERNEO individual patient data meta-analysis

Neoadjuvant SRS for Brain Metastases

INTERNEO (INTERnational collaboration of NEOadjuvant SRS for brain metastases)

- 9 institutions across 5 countries (Australia, Canada, South Korea, Switzerland, USA)

Eligibility Criteria

- Consecutive patients undergoing planned SRS prior to resection
- 2012-2023
- Any solid organ primary
- No prior local therapy to metastasis (SRS or surgery)

Endpoints: local recurrence; radionecrosis (any grade and symptomatic); leptomeningeal disease (overall and nodular)

@cristian_udo

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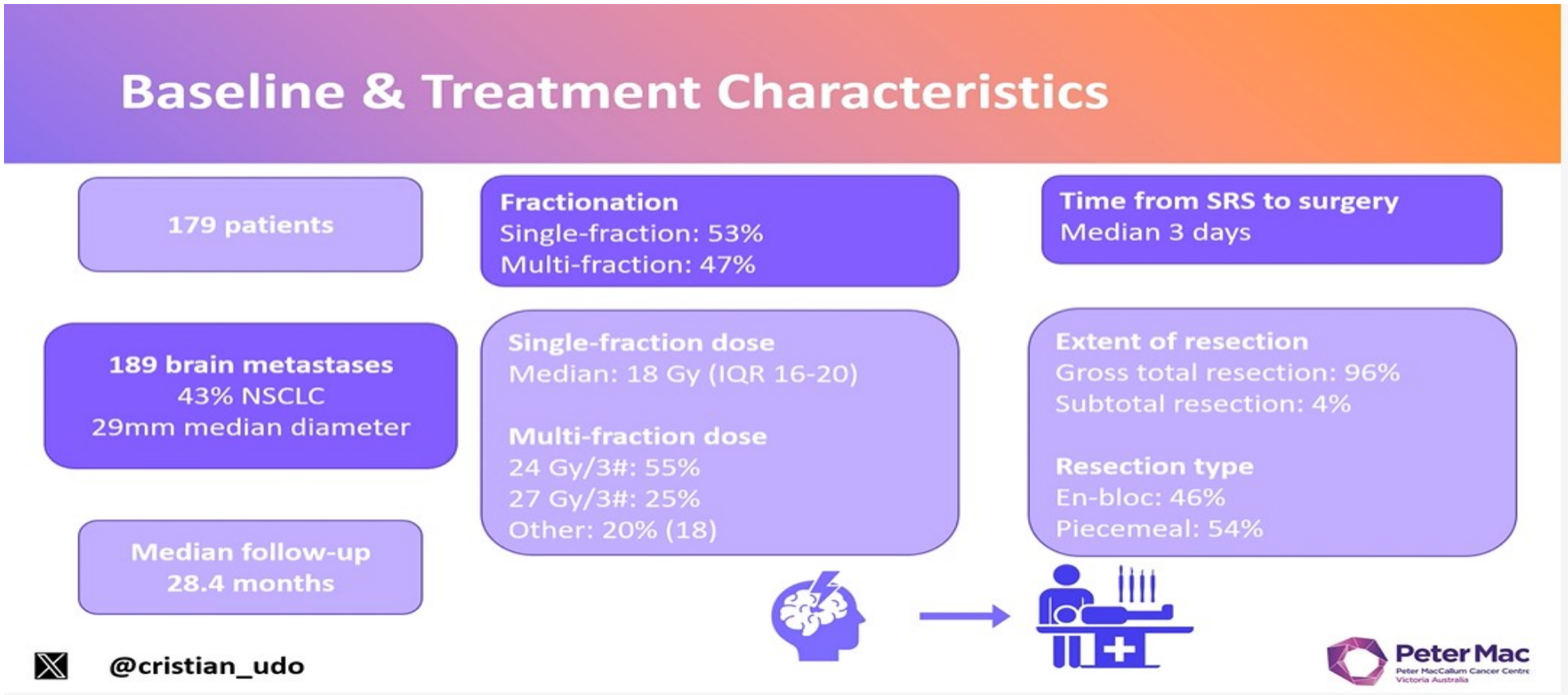
Peter MacCallum Cancer Centre
Victoria Australia

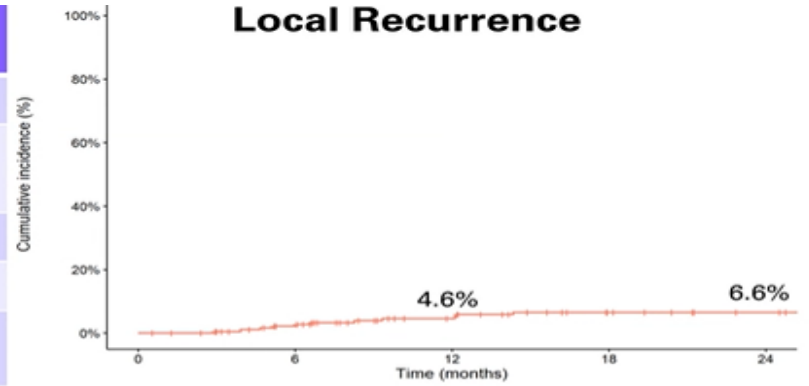
Neoadjuvant SRS for Brain Metastases

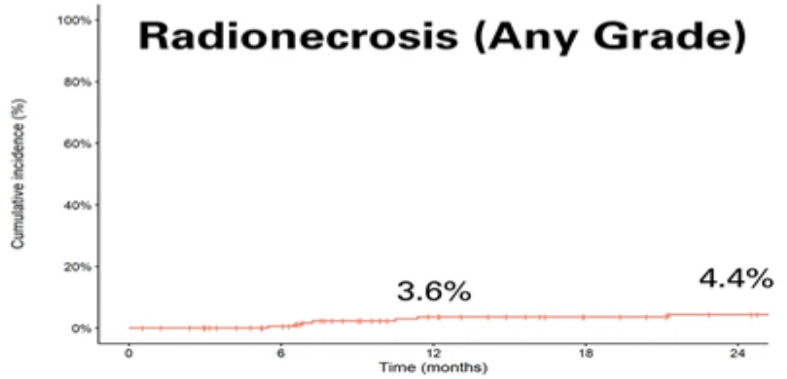


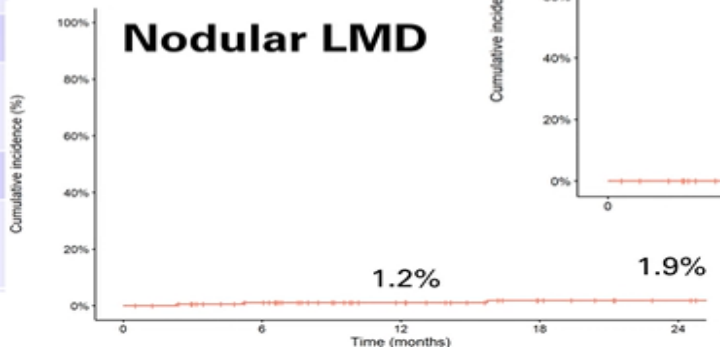
Neoadjuvant SRS for Brain Metastases

12-month (95% CI)	24-month (95% CI)
Local Recurrence	
4.6% (1.4-7.6%)	6.6% (2.8-10.3%)
Radionecrosis (any grade)	
3.6% (0.7-6.4%)	4.4% (1.2-7.5%)
Symptomatic Radionecrosis	
1.8% (0.0-3.8%)	1.8% (0.0-3.8%)
Leptomeningeal Disease	
7.2% (3.2-11.0%)	11.0% (5.9-15.7%)
Nodular Leptomeningeal Disease	
1.2% (0.0-2.7%)	1.9% (0.0-4.0%)

@cristian_udo







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Neoadjuvant SRS for Brain Metastases

INTERNEO: Summary

- Global experience
- Extended follow-up (median 28 months)
- Multi-fraction neoadjuvant SRS: high proportion (47%), largest cohort

Excellent 12-month outcomes

a) Local recurrence: 5%

b) Radionecrosis (any grade/symptomatic): 4%/2%

c) Nodular LMD: 1%

Neoadjuvant SRS for Brain Metastases

Susanne Rogers MD PhD
Radio-Onkologie-Zentrum Mittelland, Kantonsspital Aarau, Switzerland

PREOP-2: An international randomised controlled trial of preoperative *vs* postoperative SRS for brain metastases: a planned interim analysis

Inselspital E.Ermis, I.Zubak
KSGR B.Baumert, C.Zweifel
KSSG D.Brugge, M.Neidert
KSW C.Oehler, M-E.Halatsch
LUKS G.Studer
KSA O.Riesterer, C.Musahl

Innsbruck D.Minasch, J.Kerschbaumer

Kiel O.Blanck, O.Wittenstein, H.Ahmeti

Forschungsrat KSA

DEGRO ARBEITSGRUPPE RADIOCHIRURGIE/ STEREOTAXIE

DKG KREBSGESELLSCHAFT

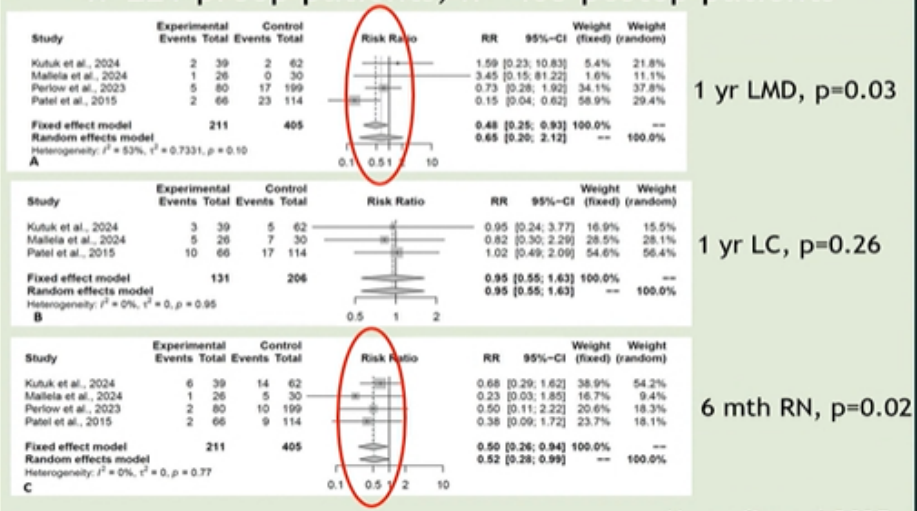
krebsliga aargau

Neoadjuvant SRS for Brain Metastases

Rationale for preoperative SRS for brain metastases

- ✔ Sterilisation of disseminated tumour cells
- ✔ More accurate target definition
- ✔ Smaller clinical and planning target margins
- ✔ Irradiated tissue subsequently resected
- ✔ Less delay to systemic therapy
- ✔ Patient convenience
- ➡ Reduction in leptomeningeal recurrence

Meta-analysis 4 comparative studies
n=221 preop patients, n= 405 postop patients



Maroufi et al 2025

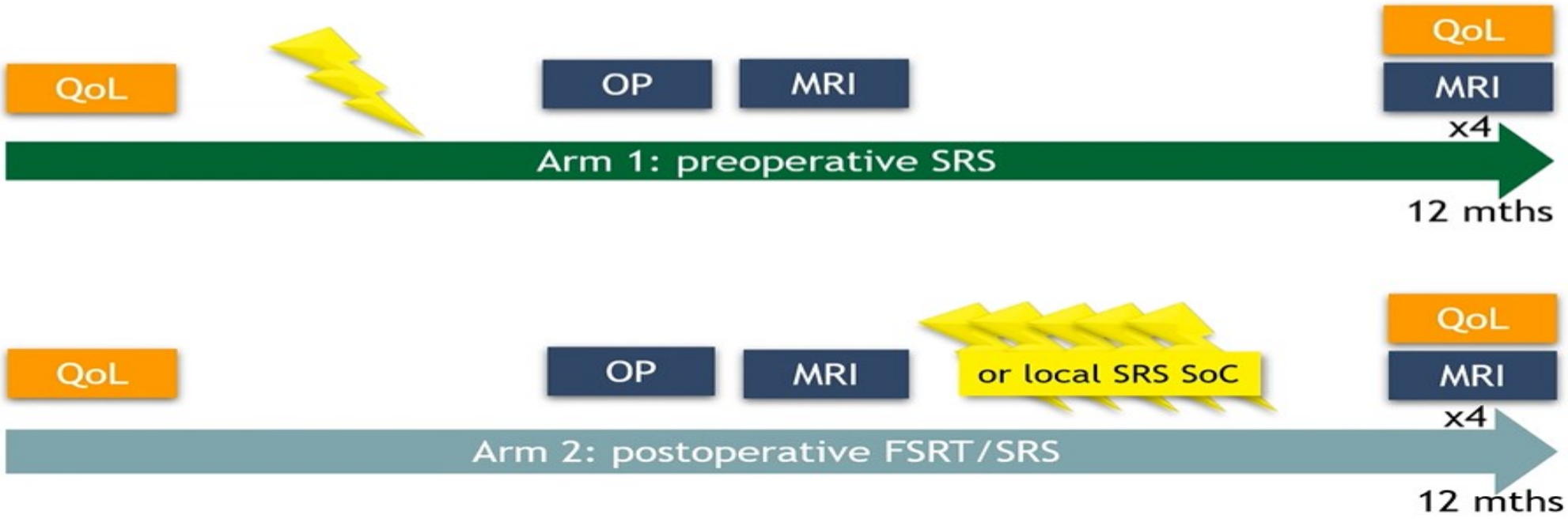
PREOP-2: a randomised international Phase III trial

Neoadjuvant SRS for Brain Metastases

Radio-Onkologie-Zentrum Mittelland

PREOP-2

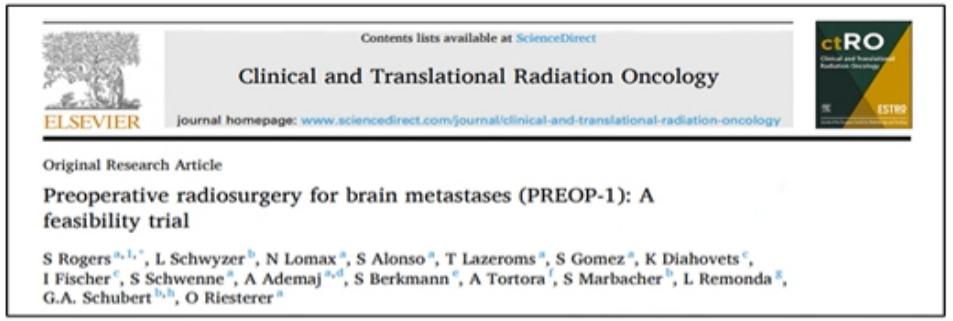
- Eligibility: BM ≤ 4 cm, predicted GTR, ≤3 BM for SRS, cancer diagnosis
- Primary endpoint: Time to leptomeningeal disease



Neoadjuvant SRS for Brain Metastases

KSA
Radio-Onkologie-Zentrum
Mittelland

Planned Interim Analysis: **Multicentre Feasibility**



Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology

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Original Research Article

Preoperative radiosurgery for brain metastases (PREOP-1): A feasibility trial

S Rogers [a,1,*], L Schwyzer [b], N Lomax [a], S Alonso [a], T Lazeroms [a], S Gomez [a], K Diahovets [c], I Fischer [c], S Schwenne [a], A Ademaj [a,d], S Berkmann [e], A Tortora [f], S Marbacher [b], L Remonda [g], G.A. Schubert [b,h], O Riesterer [a]

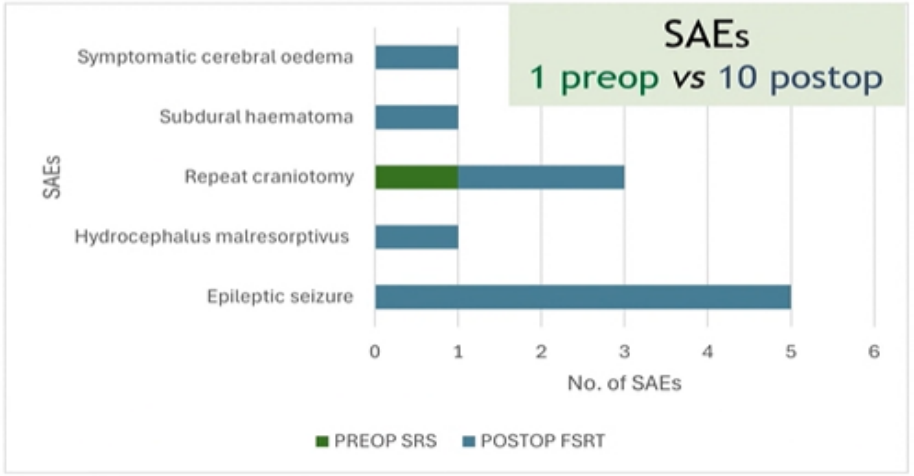
- Preoperative SRS was performed in 100% (21/21) patients in Arm 1
  - The mean interval between preoperative SRS and resection of the brain metastasis was 1.9 (± s.d. 1.94) days, which was well within the maximum of 1 week interval recommended in the protocol.
- Postoperative FSRT was delivered to 100% (19/19) patients in Arm 2
  - The mean interval to start of postoperative FSRT was 21.9 (± s.d 11.6) days, within the recommended 30 days.

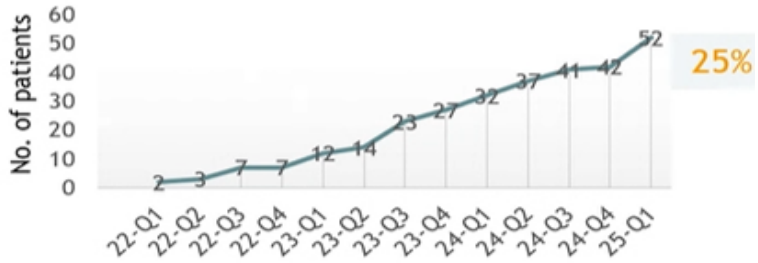
Neoadjuvant SRS for Brain Metastases

Mittelland

Planned Interim Analysis: **Toxicity**

- 11/19 SAEs were neurological (all grade 3)
- 9/11 'possibly' and 2/11 'probably' related to either SRS/FSRT or neurosurgery





Conclusions: Preoperative SRS appears safe and feasible
PREOP-2 will continue to accrue

susanne.rogers@ksa.ch

Merci.