CENTRAL NERVOUS SYSTEM

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CNS OUTLINE

1. "Here's looking at you, SCLC Whole-Brain Irradiation. Do we really need you?"
A playful twist on the famous line from the film "Casablanca."

2. "Is it better to shine the beam before or after the immunotherapy scene, to suffer or to heal in the mind's great theater?"
Shakespeare contemplation on the "slings and arrows of outrageous fortune" from Hamlet.

3. *"*To spare or not to spare, that is the question"?
Can Hippocampal Avoidance (HA) Result in Sustained Prevention of Cognitive Function during Whole Brain Radiotherapy (WBRT) for Patients with Brain Metastases?

***4.* "I can't explain what it means. And even if I could, I'm not sure I'd like it"**
Inspiration from JD Salinger – The catcher in the rye (il giovane Holden)

5. "REUNION"
Fred Uhlman

***6. "*Is procrastination of radiotherapy the thief of good time" for grade 2 glioma?**
Inspiration from Edward Young in Night-Thoughts

"Here's looking at you, SCLC Whole-Brain Irradiation. Do we really need you? “

"Here's looking at you, SCLC Whole-Brain Irradiation. Do we really need you? "

- The phase III EORTC trial (2007) established the role of PCI in ES-SCLC patients with a response to chemotherapy (pre-brain imaging not mandatory)
- Takahashi et al. (Lancet O 2017) compared PCI and MRI surveillance → PCI did not prolong OS, despite that it reduced the risk of brain mets development from 59.0 to 32.9% at 1-year
- Keller et al (Clin Lung Cancer 2021) → active MRI surveillance and prompt salvage radiation for brain metastases is feasible in ES-SCLC
- CASPIAN and IMpower133 trials → decreases in brain mets rates in ES- SCLC with chemoimmunotherapy vs chemotherapy alone.
- **CROSS-FIRE trial (2023)** → After SRS, SCLC shorter OS compared to NSCLC.
  CNS progression occurred earlier in SCLC pts overall but was similar in patients matched on baseline factors.
  SCLC was not associated with increased neurological mortality, number of lesions at CNS progression, or leptomeningeal progression
- Various aspects of SCLC management have changed: staging with PET and brain MRI, modern radiotherapy techniques and intensive thoracic radiotherapy.

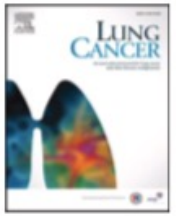
"Here's looking at you, SCLC Whole-Brain Irradiation. Do we really need you? "

- **U.S. and European guidelines** → for ES-SCLC pts showing response to initial systemic therapy, baseline brain MRI evaluation and regular brain MRI surveillance are recommended

- Various aspects of SCLC management have changed: staging with PET and brain MRI, modern radiotherapy techniques and intensive thoracic radiotherapy.

"Here's looking at you, SCLC Whole-Brain Irradiation. Do we really need you? "

Use of radiation therapy among patients with Extensive-stage Small-cell lung cancer receiving Immunotherapy: Canadian consensus recommendations



- All patients who respond to concurrent chemo-immunotherapy should undergo restaging with brain MRI to guide decision-making regarding PCI versus MRI surveillance alone.
- MRI surveillance should be conducted for 2 years after response to initial therapy.
- PCI (e.g., 25 Gy in 10 fractions or 20 Gy in 5 fractions) can be considered for patients without CNS involvement who have a response to chemo-IT and good PS.
- Concurrent treatment with PCI and immunotherapy or with TRT, PCI, and IT is appropriate after completion of initial therapy.

Table 1. Ongoing clinical trials evaluating prophylactic cranial irradiation and its alternatives in small cell lung cancer.

Trial	Phase	SCLC stage	Surgical resection	Immunotherapy	Hippocampal avoidance	Cognitive preservation drugs	Study Arm(s): E) Experimental; C) Control	Primary End points	Notable secondary and exploratory end points	Estimated no. of enrolment	Start Date - Estimated completion date
SWOG S1827 (MAVERICK)/ NCT04155034	III	Limited stage & Extensive stage	allowed	allowed	allowed	not mentioned	Arm E: MRI surveillance alone Arm C: PCI & MRI surveillance	OS	BMFS; CFFS	668	January 2020 – November, 2027
EORTC PRIMALung/ NCT04790253	III	Limited stage & Extensive stage	allowed	stratification variable	allowed	memantine allowed	Arm E: MRI surveillance alone Arm C: PCI & MRI surveillance	OS	OS and CFFS according to stage/ immunotherapy/ HA/memantine use; BMFS; QoL	600	July 2022– April 2028
NRG CC003/ NCT02635009	II/III	Limited stage and Extensive stage	allowed	not mentioned	mandated in Arm E	memantine: stratification variable	Arm E: HA-PCI (IMRT) Arm C: PCI (3DCRT)	BMFS (Phase II); Cognitive deterioration status	OS; QoL; BMFS (Phase III)	418	December 2015– April 2027
NCT04829708	III	Limited stage	not allowed	not mentioned	Recommended in Arm C	not mentioned	Arm E: MRI surveillance alone Arm C: PCI & MRI surveillance	OS	PFS; BMFS; cognitive impairment incidence	534	April 2021–April 2028
NCT03514849	III	Limited stage (resected pT1–2N0M0)	mandated	not mentioned	not mentioned	not mentioned	Arm E: Surgery and chemotherapy and PCI Arm C: Surgery & chemotherapy	5-year OS	5-year DFS; OS	360	August 2018– March 2026
NCT04535739	III	Extensive stage	NA	not mentioned	not mentioned	not mentioned	Arm E: Thoracic RT and PCI Arm C: Thoracic RT & surveillance	2-year OS	2-year BMFS; 2-year PFS	414	July 2019– June 2022
NCT02605811	II	Limited stage	not mentioned	not mentioned	not mentioned	not mentioned	Arm E: Temozolomide Arm C: PCI	2-year BMFS	NA	426	September 2015– December 2021
NCT03995667	II	Limited stage and Extensive stage	not allowed	not mentioned	NA	not mentioned	Arm E: tumour treating fields therapy (BM prevention)	BM rate at 6 months	OS; BMFS; QoL; AE	106	June 2019–June 2024
NCT04947774	Prospective cohort study	Extensive stage	NA	mandated	not mentioned	not mentioned	Arm E: MRI surveillance alone Arm C: PCI & MRI surveillance	BMFS	PFS; OS;	100	November 2020– October, 2022

"Here's looking at you, SCLC Whole-Brain Irradiation. Do we really need you? "

MRI surveillance is now an acceptable alternative to PCI in ES-SCLC

SRS feasible

"Is it better to shine the beam before or after the IT scene, to suffer or to heal in the mind's great theater?“

IT - SRS for METS

"Is it better to shine the beam before or after the IT scene,
to suffer or to heal in the mind's great theater?"

IT - SRS for METS

Concurrent Administration of Immune Checkpoint Inhibitors and Single Fraction Stereotactic Radiosurgery in Patients With Non-Small Cell Lung Cancer, Melanoma, and Renal Cell Carcinoma Brain Metastases

INTERNATIONAL JOURNAL OF
RADIATION ONCOLOGY • BIOLOGY • PHYSICS

Leherer IJROBP 2023

"Is it better to shine the beam before or after the IT scene,
to suffer or to heal in the mind's great theater?"

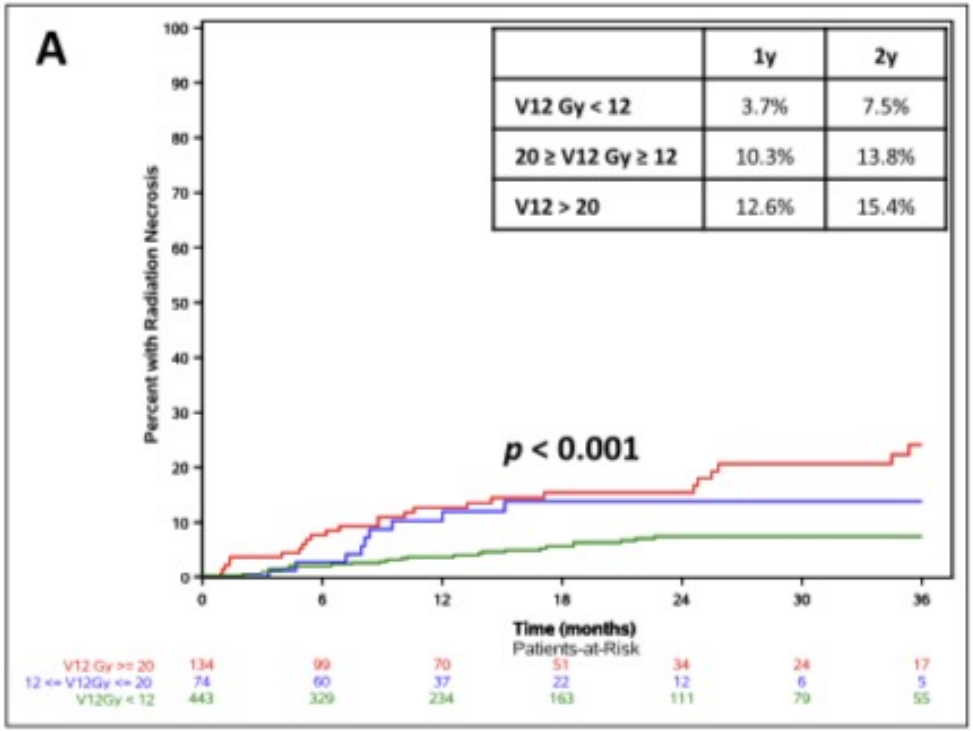
IT - SRS for METS

657 pts with 4182 brain mets across 11 international institutions

Mets from NSCLC, renal cell carcinoma, or melanoma treated with SRS and ICI

- **SRS and ICI → low risk of any grade RN and SRN (not increased with concurrent administration)**
- **Therefore, ICI can safely be administered within 4-weeks of SRS.**
- **3 risk groups based on V12 Gy were identified**
  (1) < 12 cm3 → 3.7%
  (2) 20 cm3 ≥ V12 Gy ≥ 12 cm3 → 10.3%
  (3) > 20 cm3 → 12.6%

  V12 Gy ≥ 12 cm3 was also predictive of increased SRN



	1y	2y
V12 Gy < 12	3.7%	7.5%
20 ≥ V12 Gy ≥ 12	10.3%	13.8%
V12 > 20	12.6%	15.4%

"Is it better to shine the beam before or after the IT scene,
to suffer or to heal in the mind's great theater?"

IT - SRS for METS

Brain metastases and next-generation anticancer therapies: a survival guide for clinicians

Critical Reviews in Oncology / Hematology 194 (2024) 104239

Fig. 1. Suggested therapeutic considerations for NSCLC with asymptomatic and active CNS disease in a multidisciplinary tumor board discussion.

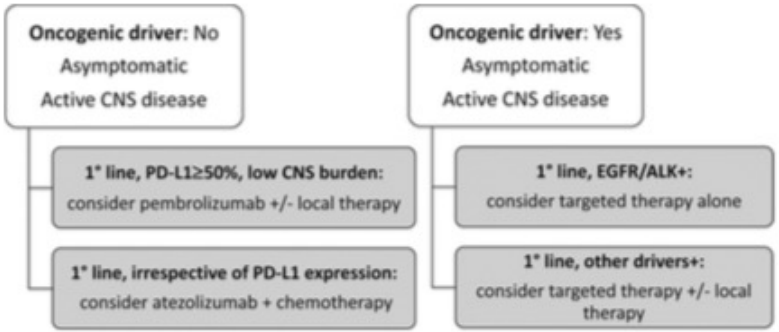
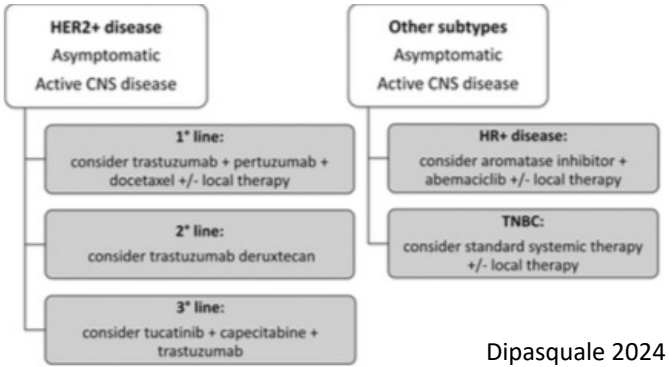


Fig. 2. Suggested therapeutic considerations for breast cancer with asymptomatic and active CNS disease in a multidisciplinary tumor board



Dipasquale 2024

Neuro-Oncology

24(3), 331–357, 2022 | https://doi.org/10.1093/neuonc/noab262 | Advance Access date 21 December 2021

Treatment for Brain Metastases: ASCO-SNO-ASTRO Guideline

Recommendation 1.2.
Where surgery is considered, no recommendation regarding the method of resection (piecemeal *v* en bloc) can be made (Type: informal consensus; Evidence quality: low; Strength of recommendation: none).

Recommendation 1.3.
No recommendation can be made for or against laser interstitial thermal therapy (Type: informal consensus; Evidence quality: low; Strength of recommendation: none).

Recommendation 2.1.
Patients with symptomatic brain metastases should be offered local therapy (radiosurgery/radiation therapy and/or surgery) as recommended in this guideline regardless of the systemic therapy used for the systemic disease (Type: evidence-based; Evidence quality: high; Strength of recommendation: strong).

Recommendation 2.2.
For patients with asymptomatic brain metastases, local therapy should not be deferred unless deferral is specifically recommended in recommendations 2.3 through 2.7 of this guideline. The decision to defer local therapy should be based on a multidisciplinary discussion (neuro- or medical oncology, neurosurgery, and radiation oncology) of the potential benefits and harms the patient may experience (Type: evidence-based; Evidence quality: high; Strength of recommendation: strong).

Recommendation 2.3.
Osimertinib or icotinib may be offered to patients with asymptomatic brain metastases from *EGFR*-mutant non–small-cell lung cancer (NSCLC). If these agents are used, local therapy may be delayed until there is evidence of intracranial progression (Type: informal consensus; Evidence quality: low; Strength of recommendation: weak).

Local therapy should not be deferred unless deferral is specifically recommended.

The decision to defer local therapy should be based on a multidisciplinary discussion of the potential benefits and harms the patient may experience

Evidence quality: low; Strength of recommendation: weak). *NOTE: See Recommendation 2.2 regarding local therapy.*

Recommendation 2.6.
Ipilimumab plus nivolumab (for all patients regardless of *BRAF* status) or dabrafenib plus trametinib (for patients with *BRAF*-V600E mutation) may be offered to patients with asymptomatic brain metastases from melanoma. If these agents are used, local therapy may be delayed until there is evidence of intracranial progression (Type: informal consensus; Evidence quality: low; Strength of recommendation: weak).

- Osimertinib or Icotinib → **asympto EGFR-m NSCLC mets**
- Alectinib, brigatinib, or ceritinib –> **asympto ALK-rearranged NSCLC mets**
- Pembrolizumab → from immunotherapy-naïve, **programmed death-ligand 1–NSCLC** who are also receiving pemetrexed and a platinum agent
- Ipilimumab plus nivolumab (regardless of BRAF status) or dabrafenib plus trametinib (with BRAF-V600E mutation) → **asympto melanoma mets**
- combination of tucatinib, trastuzumab, and capecitabine → **human epidermal growth factor receptor 2–positive breast cancer mets** who have asymptomatic brain metastases and have progressed on previous trastuzumab, pertuzumab, and/or trastuzumab emtansine–based therapy.

Type: evidence-based; Evidence quality: low; Strength of recommendation: weak

Recommendation 3.5.
Memantine and hippocampal avoidance should be offered to patients who will receive WBRT and have no hippocampal lesions and 4 months or more expected survival (Type: evidence-based; Evidence quality: high; Strength of recommendation: strong).

To spare or not to spare, that is the question"?

To spare or not to spare, that is the question"?

- RTOG0933 and NRG CC001 demonstrated that HA-WBRT is associated with the preservation of neurocognitive functions and QoL

In SCLC, the neurocognitive benefits of HA-PCI are not conclusive:

- Phase III PREMER RCT (150 pts LS-SCLC and ES-SCLC) → significantly improved neurocognitive functions in the HA-PCI group
- phase III RCT (NCT01780675), 168 patients LS-SCLC and ES-SCLC, no differences (different neurocognitive assessment methods employed)

To spare or not to spare, that is the question"?

Neuro-Oncology

XX(XX), 1–11, 2023 | https://doi.org/10.1093/neuonc/noad226 | Advance Access date 9 December 2023

Evaluating the heterogeneity of hippocampal avoidant whole brain radiotherapy treatment effect: A secondary analysis of NRG CC001

Hua-Ren R. Cherng, Kai Sun, Søren Bentzen, Terri S. Armstrong, Vinai Gondi, Paul D. Brown, Minesh Mehta, and Mark V. Mishra

To spare or not to spare, that is the question"?

Differential neuroprotective response to HA-WBRT was identified
derived benefit from HA-WBRT

Pts surviving ≥ 4 months

Pts with less severe patient-reported cognitive impairment at baseline

Pts with primary lung histology.

To spare or not to spare, that is the question"?

Neuro-Oncology
25(1), 167–176, 2023 | https://doi.org/10.1093/neuonc/noac148 | Advance Access date 31 May 2022
https://doi.org/10.1093/neuonc/noac148

Hippocampal avoidance prophylactic cranial irradiation (HA-PCI) for small cell lung cancer reduces hippocampal atrophy compared to conventional PCI

- HA-PCI reduced hippocampal atrophy compared to conventional PCI.
- Hippocampal atrophy was not directly associated with memory decline.
- Both HA-PCI and PCI were associated with considerable brain injury and aging.

To spare or not to spare, that is the question"?

Neuro-Oncology
25(7), 1323–1330, 2023 | https://doi.org/10.1093/neuonc/noad029 | Advance Access date 3 February 2023

Whole-brain radiotherapy associated with structural changes resembling aging as determined by anatomic surface-based deep learning

Nikhil Rammohan, Alexander Ho, Pierre Besson, Tim J. Kruser, S. Kathleen Bandt

Results: 4220 subjects were analyzed (4148 healthy controls and 72 patients). The median radiation dose was 30 Gy (range 25–37.5 Gy). The whole brain and substructures underwent structural change resembling rapid aging in radiated patients compared to healthy controls; the whole brain "aged" 9.32 times faster, the cortex 8.05 times faster, the subcortical structures 12.57 times faster, and the hippocampus 10.14 times faster. In a subset analysis, the hippocampus "aged" 8.88 times faster in patients after conventional WBRT versus after hippocampal avoidance (HA)-WBRT.

Conclusions: Our findings suggest that WBRT causes the brain and its substructures to undergo structural changes at a pace up to 13x of the normal aging pace, where hippocampal avoidance offers focal structural protection. Correlating these structural imaging changes with neurocognitive outcomes following WBRT or HA-WBRT would benefit from future analysis.

To spare or not to spare, that is the question"?

Recommendation 3.5.
Memantine and hippocampal avoidance should be offered to patients who will receive WBRT and have no hippocampal lesions and 4 months or more expected survival (Type: evidence-based; Evidence quality: high; Strength of recommendation: strong).

Current status and perspectives of interventional clinical trials for brain metastases: analysis of ClinicalTrials.gov

133 phase II
35 phase III
BM from lung, breast cancer and melanoma
113 → tyrosine kinase inhibitors (more frequently Osimertinib, Icotinib and Pyrotinib)
50 → monoclonal antibodies (more frequently Trastuzumab, Pembrolizumab, Nivolumab)
20 → conventional chemotherapies
6 → no oncological active drugs

96 → RT → 54 as exclusive treatment and 42 in combination with systemic therapies.

Tini et al., Radiat Oncol 2023

Brain Mets. Future perspective

Trials.gov

	n° trials
Radiotherapy	
Stereotactic radiotherapy (SRS/SRT)	47
Whole-brain RT (WBRT)	27
Hippocampal avoidance WBRT (HA-WBRT)	10
IORT	1
Brachytherapy	1
Technique not specified	10

“I can’t explain what it means. And even if I could, I’m not sure I’d like it“

Inspiration from JD Salinger – The catcher in the rye (il giovane Holden)

"I can't explain what it means. And even if I could, I'm not sure I'd like it"

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RANO 2.0: Update to the Response Assessment in Neuro-Oncology Criteria for High- and Low-Grade Gliomas in Adults

J Clin Oncol 41:5187-5199

"I can't explain what it means. And even if I could, I'm not sure I'd like it"

Inspiration from JD Salinger – The catcher in the rye (il giovane Holden)

The same imaging protocol at baseline and across all time points

RANO-HGG, the product of the maximal cross-sectional diameters of the enhancing lesions will be used to determine the size of contrast-enhancing lesions.

RANO-LGG, the maximal cross-sectional T2-weighted fluid-attenuated inversion recovery (FLAIR) diameters will be used to determine the size of non–contrast-enhancing lesions

"I can't explain what it means. And even if I could, I'm not sure I'd like it"

Inspiration from JD Salinger – The catcher in the rye (il giovane Holden)

To date no conclusive benefit of volumetric analysis over two-dimensional measurement (except IDHm diffuse glioma)

The first postradiotherapy MRI as the baseline for newly diagnosed gliomas

Pseudoprogression is high in the first 12 weeks after chemoradiotherapy for glioblastomas (occurring in up to 30%-40% of patients)

For IDH-mutated gliomas and other glial tumors, the time course for pseudoprogression can extend well beyond 3 months.

Advanced imaging techniques including perfusion imaging (dynamic susceptibility contrast or dynamic contrast-enhanced MRI), diffusion imaging, magnetic resonance spectroscopy, and amino acid positron emission tomography may help predict tumor response or allow the differentiation of pseudoprogression from progression.

There is also increasing interest in the use of automated assessment of response and the use of artificial intelligence.

→ are undergoing validation studies and may eventually be incorporated into the RANO criteria.

"REUNION"

Fred Uhlman

"REUNION"

Fred Uhlman

PET-based response assessment criteria for diffuse gliomas (PET RANO 1.0): a report of the RANO group

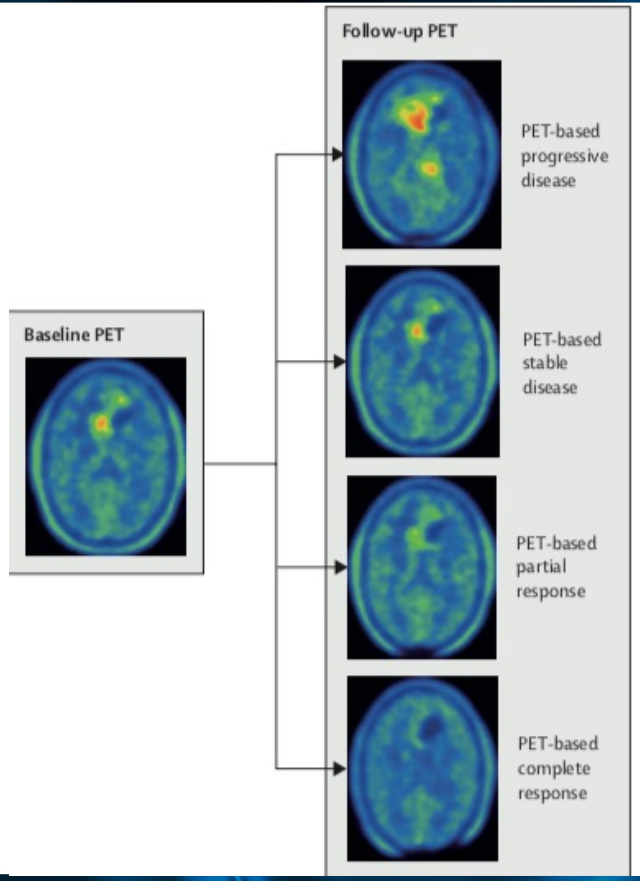
Nathalie L Albert, Norbert Galldiks, Benjamin M Ellingson, Martin J van den Bent, Susan M Chang, Francesco Cicone, John de Groot, Eng-Siew Koh, Ian Law, Emilie Le Rhun, Maximilian J Mair, Giuseppe Minniti, Roberta Rudà, Andrew M Scott, Susan C Short, Marion Smits, Bogdana Suchorska, Nelleke Tolboom, Tatjana Traub-Weidinger, Joerg-Christian Tonn, Antoine Verger, Michael Weller, Patrick Y Wen, Matthias Preusser

Lancet Oncol 2024; 25: e29-41

	Tracer	Tumour type	n	Study type	Diagnosis or recurrence	Timepoints (baseline and follow-up)	Thresholds	Parameters	Therapy	Previous treatment	Clinical endpoints
(Continued from previous page)											
Wirsching et al (2021)[12]	[^{18}F]FET	Glioblastoma (individuals older than 65 years)	67	Post-hoc analysis of a prospective trial	Diagnosis or after first surgery	Baseline (pretreatment), follow-up (4 weeks after completion of radiotherapy)	Cutoffs for TBR established by ROC analysis but not reported	Absolute TBR at baseline and follow-up	Bevacizumab plus hypofractionated radiotherapy	Surgery	High pretreatment TBR in contrast-enhancing tumour regions was associated with overall survival independent of the treatment arm (HR 2·53, 95% CI 1·17–5·49). MRI contrast-enhancing volume, and ADC (HR 3·54, 95% CI 1·12–11·16); high TBR at first follow-up (on treatment) in contrast-enhancing tumour regions was associated with longer overall survival in the radiotherapy arm (p=0·44; median survival not reported)
Werner et al (2021)[13]	[^{18}F]FET	Glioblastoma	23	Retrospective	Diagnosis or after first surgery	Baseline (after radiotherapy)	TBR_{max} <1·95 at baseline	Absolute TBR_{max} at baseline, relative changes of TBR_{max} and dynamic parameters	No treatment (follow-up)	Surgery, radiotherapy, temozolomide, and lomustine (according to the CeTeG/NOA-09 trial)[14]	Accuracy of 87% in identifying pseudoprogression at a TBR_{max} <1·95 (p=0·029), with improved accuracy (91%) when integrating relative changes and specificity (100%) with dynamic parameters
Beppu et al (2022)[15]	[^{11}C]MET	IDH-mutant, lower-grade glioma (grades 2 or 3)	30	Not reported	Diagnosis or after first surgery	Baseline (after adjuvant temozolomide)	TBR_{max} ≥1·27 at baseline	TBR_{max} at baseline	No treatment (follow-up)	Surgery, and temozolomide with or without radiotherapy	TBR_{max} ≥1·27 associated with shorter progression-free survival (univariate log-rank p<0·002; multivariate HR 8·44; p=0·002)
Wollring et al (2023)[16]	[^{18}F]FET	Diffuse glioma (grades 3 or 4)	36	Retrospective	Recurrence or progression	Baseline and follow-up (not later than 2 cycles of chemotherapy)	Cutoffs for relative changes established with ROC analysis (progression-free survival: MTV 0%, TBR_{max} 0%, TBR_{mean} 0%, and time to progression −7%; overall survival: MTV 0%, TBR_{max} −47%, TBR_{mean} 0%, and time to progression −7%).	TBR_{max}, TBR_{mean}, MTV, time to progression, and new hotspot with a TBR_{max} >1·6	Lomustine, or lomustine or procarbazine	At least one line of pretreatment including resection, radiotherapy, and alkylating chemotherapy, or combinations of the three	Multivariate analysis (progression-free survival): TBR_{max} change (HR 2·909; p=0·029), MTV change (HR 4·546; p=0·001), new hotspots (HR 3·155; p=0·019); multivariate analysis (overall survival): new hotspots (HR 8·578; p<0·001); all independent from MRI-based RANO criteria, TBR_{max} change, and time to progression change
Darcourt et al (2023)[17]	[^{18}F]-FDOPA	Diffuse glioma (grades 3 or 4)	107	Prospective	Recurrence or progression	Baseline (once after inconclusive MRI during follow-up)	Cutoff for PD according to ROC analysis: TBR_{max} of 1·94	TBR_{max} and TSR_{max}	No treatment (follow-up)	Surgery with or without radiotherapy and chemotherapy	Tumour board decision changed in 26·8% of participants (diagnosis) and 22·5% of participants (management) if PET was considered; sensitivity (86% vs 83%), specificity (64% vs 58%), and accuracy (71% vs 66%) all higher if PET was considered

ADC=Apparent diffusion coefficient. [^{11}C]MET=^{11}C-methionine. [^{18}F]-F-DOPA=^{18}F-dihydroxy-fluoro-L-phenylalanine. [^{18}F]FET=^{18}F-fluoroethyl-L-tyrosine. HR=hazard ratio. MGMT=O^6-methylguanine-DNA-methyltransferase. MTV=metabolic tumour volume. NA=not available. OR=odds ratio. PD=progressive disease. RANO=Response Assessment in Neuro-Oncology. ROC=receiver operating characteristics. SUV=standardised uptake value. TBR=tumour-to-background ratio. TSR=tumour-to-striatum ratio. *As defined by a priori threshold of tumour volume change ≥10%.

Table 1: **Overview of published data on amino acid PET tracers in gliomas**



"REUNION"

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[18F]FET
[11C]MET
[18F]F-DOPA

Standardised protocol

PET imaging intervals of 2–3 months, preferentially in parallel to MR imaging.

Systematic studies are needed to validate and refine the PET RANO 1.0 criteria in future updates.

"Is procrastination of radiotherapy the thief of good time?"

Inspiration from Edward Young in Night-Thoughts

"Is procrastination of radiotherapy the thief of good time?"

Inspiration from Edward Young in Night-Thoughts

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 17, 2023 VOL. 389 NO. 7

Vorasidenib in IDH1- or IDH2-Mutant Low-Grade Glioma

I.K. Mellinghoff, M.J. van den Bent, D.T. Blumenthal, M. Touat, K.B. Peters, J. Clarke, J. Mendez, S. Yust-Katz, L. Welsh, W.P. Mason, F. Ducray, Y. Umemura, B. Nabors, M. Holdhoff, A.F. Hottinger, Y. Arakawa, J.M. Sepulveda, W. Wick, R. Soffietti, J.R. Perry, P. Giglio, M. de la Fuente, E.A. Maher, S. Schoenfeld, D. Zhao, S.S. Pandya, L. Steelman, I. Hassan, P.Y. Wen, and T.F. Cloughesy, for the INDIGO Trial Investigators*

"Is procrastination of radiotherapy the thief of good time?"

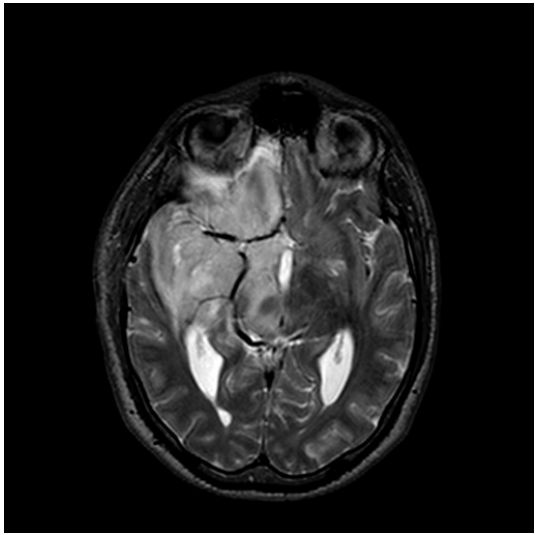
Inspiration from Edward Young in Night-Thoughts

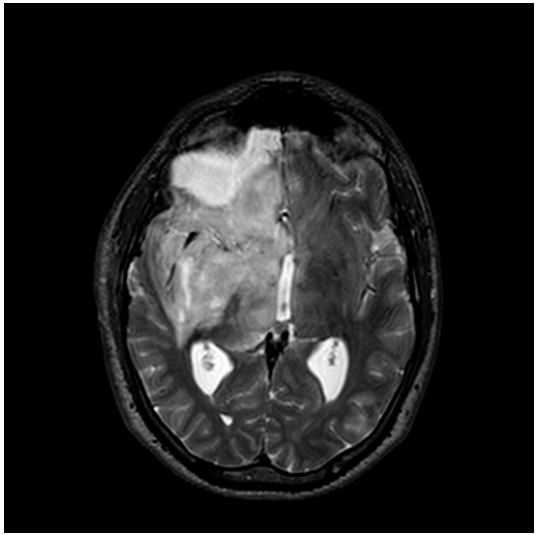
Diffuse gliomas with IDH mutation

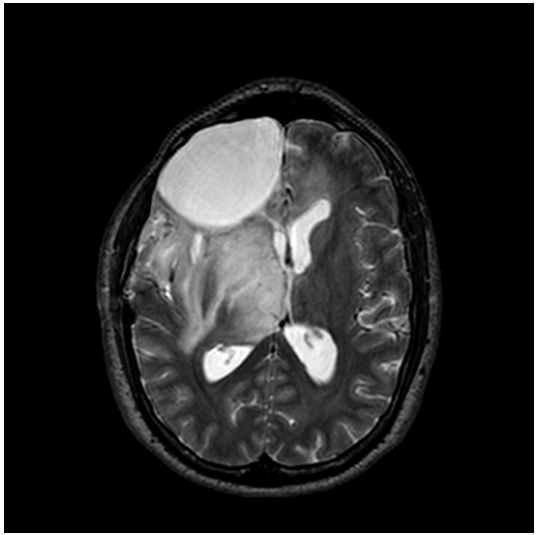
most common malignant primary brain tumors in adults younger than 50 years of age,

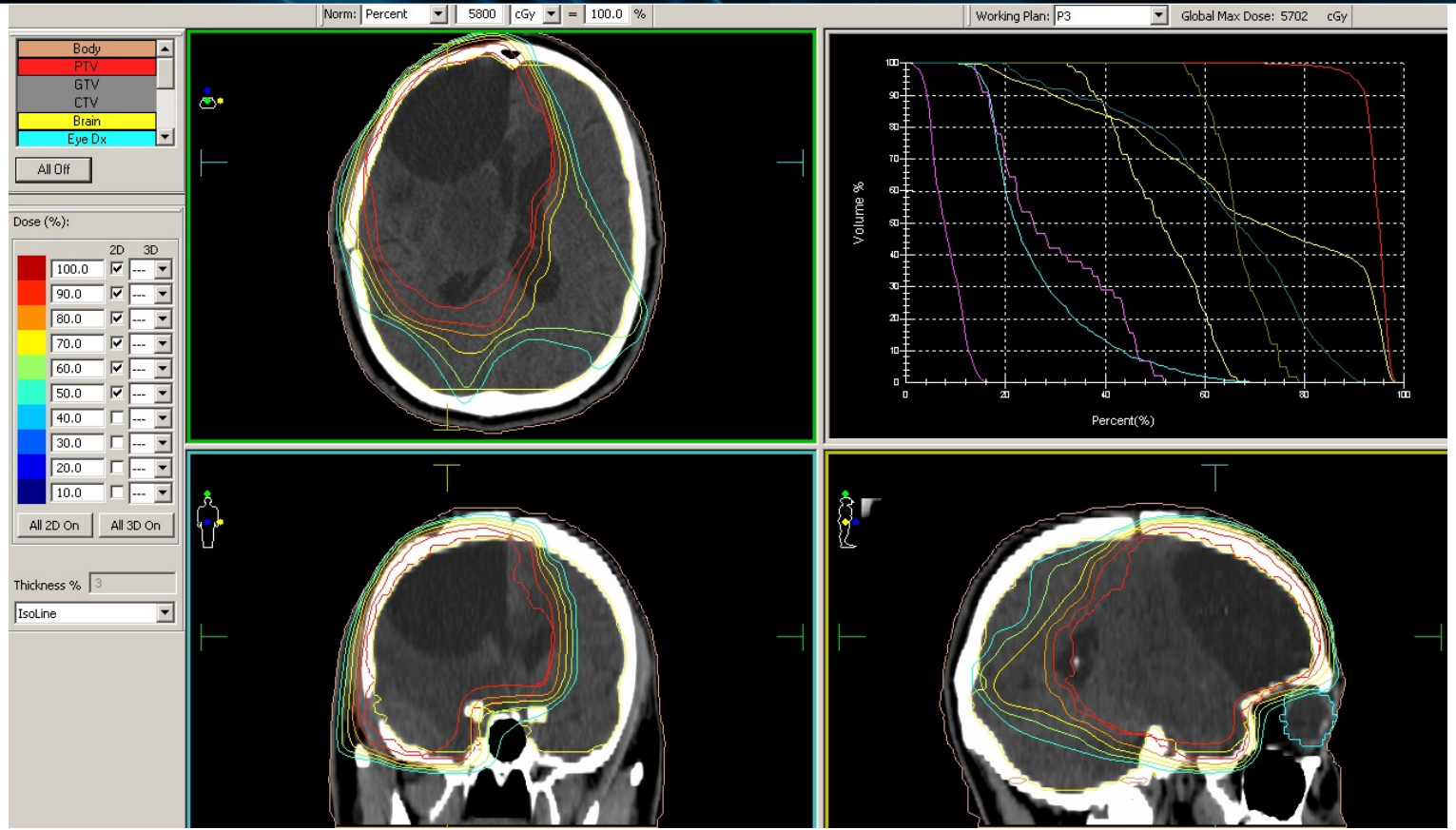
are not curable with current therapies,

continuously grow and infiltrate normal brain tissue in the absence of treatment.








Norm: Percent 5800 cGy = 100.0 %
Working Plan: P3 Global Max Dose: 5702 cGy
Body
PTV
GTV
CTV
Brain
Eye Dx
All Off
Dose (%):
2D 3D
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
All 2D On
All 3D On
Thickness % 3
IsoLine
Volume %
Percent(%)

"Is procrastination of radiotherapy the thief of good time?"

Inspiration from Edward Young in Night-Thoughts

double-blind, phase 3 trial, randomized
patients with residual or recurrent grade 2 IDH-mutant glioma no previous treatment other than surgery

either oral vorasidenib (40 mg once daily) or matched placebo in 28-day cycles.

- primary end point was imaging-based PFS
- secondary end point was the time to the next anticancer intervention.

"Is procrastination of radiotherapy the thief of t

Inspiration from Edward Young in Night-T

In patients with grade 2 IDH-mutant glioma (astro adn ODG)

vorasidenib significantly improved PFS and delayed the time to the next intervention. (INDIGO ClinicalTrials.gov number, NCT04164901.)

Median FUP 14 months

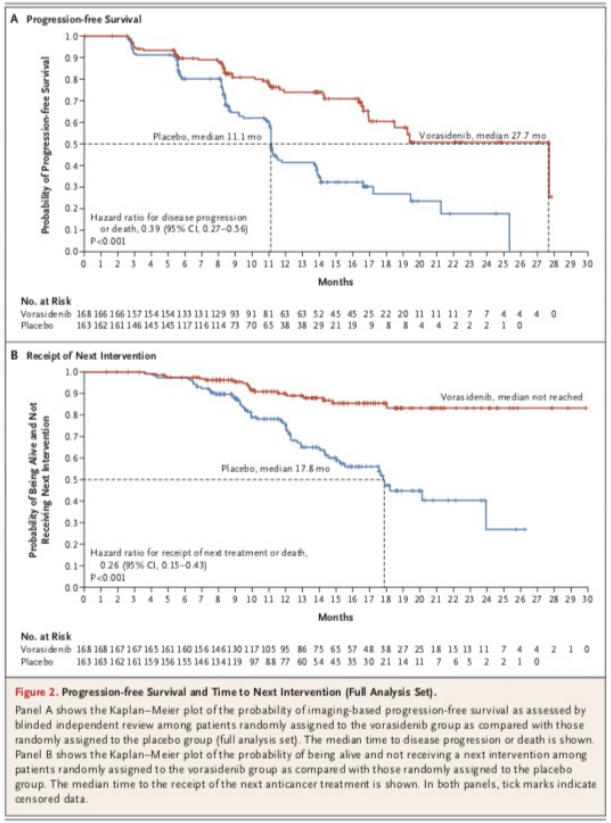


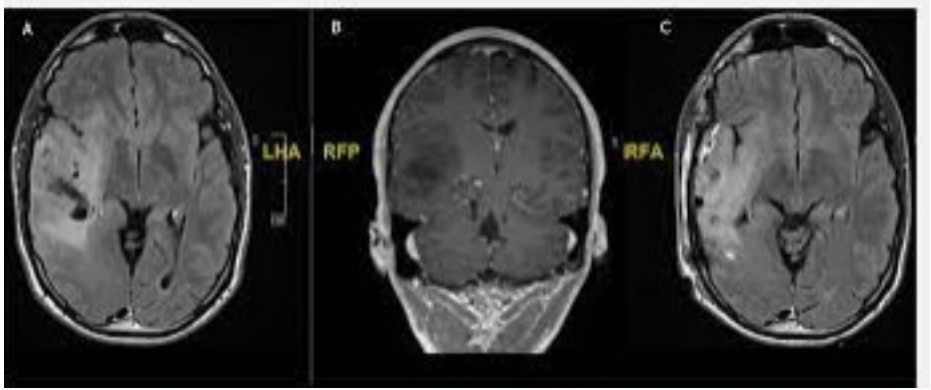
Figure 2. Progression-free Survival and Time to Next Intervention (Full Analysis Set).

Panel A shows the Kaplan–Meier plot of the probability of imaging-based progression-free survival as assessed by blinded independent review among patients randomly assigned to the vorasidenib group as compared with those randomly assigned to the placebo group (full analysis set). The median time to disease progression or death is shown. Panel B shows the Kaplan–Meier plot of the probability of being alive and not receiving a next intervention among patients randomly assigned to the vorasidenib group as compared with those randomly assigned to the placebo group. The median time to the receipt of the next anticancer treatment is shown. In both panels, tick marks indicate censored data.

AEs of grade 3 or higher were more common in the vorasidenib group than in the placebo group

serious adverse events and discontinuations of vorasidenib or placebo were low.

Effects on seizure QoL and neurocognition not yet available



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Whether 'tis nobler for the radiation oncologist's mind to suffer the slings and arrows of outdated methods
or to embrace a sea of algorithms and, by opposing, enhance precision."

Real-world Artificial Intelligence Power

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Large language models can help us to investigate at a scale not previously possible

AAPM's 2023 annual meeting

GRAZIE