Brain and spine tumours

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Disclosure : Zeiss , AB medica

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9	Sanmamed et al	Low-Dose Radiation Therapy in the Management of Coronavirus Disease 2019 (COVID-19) Pneumonia (LOWRAD-Cov19): Preliminary Report
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Rank	Author	Title
1	Soyfer et al	COVID-19 Vaccine-Induced Radiation Recall Phenomenon
2	Sahgal et al	Spinal Cord Dose Tolerance to Stereotactic Body Radiation Therapy
3	Papachristofilou et al	Low-Dose Radiation Therapy for Severe COVID-19 Pneumonia: A Randomized Double-Blind Study
4	Hall et al	NRG Oncology Updated International Consensus Atlas on Pelvic Lymph Node Volumes for Intact and Postoperative Prostate Cancer
5	Redmond et al	Stereotactic Radiosurgery for Postoperative Metastatic Surgical Cavities: A Critical Review and International Stereotactic Radiosurgery Society (ISRS) Practice Guidelines
6	Grimm et al	High Dose per Fraction, Hypofractionated Treatment Effects in the Clinic (HyTEC): An Overview
7	Schumacher et al	Effects of Exercise During Radiation Therapy on Physical Function and Treatment-Related Side Effects in Men With Prostate Cancer: A Systematic Review and Meta-Analysis

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Benign tumours : meningiomas

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CLINICAL INVESTIGATION

Hypofractionated Radiosurgery for Large or in Critical-Site Intracranial Meningioma: Results of a Phase 2 Prospective Study

Valentina Pinzi, MD,[*,†] Marcello Marchetti, MD,[*] Anna Viola, MD,[*,†,‡] Irene Tramacere, PhD,[§] Irene Cane, BSc,[*] Cecilia Iezzoni, PsyD,[*] and Laura Fariselli, MD[*]

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Purpose: Radiosurgery is a well-known, safe, and effective technique used in the treatment of intracranial meningiomas. However, single-fraction radiosurgery can lead to high toxicity rates when large-volume or critically located lesions are targeted. Multisession—also called hypofractionated—radiosurgery (hypo-RS) might overcome these limitations. Accordingly, we carried out a prospective phase 2 trial, aiming to establish whether a fractionated RS schedule of 25 Gy in 5 fractions would be safe and effective in treating large (≥ 3 cm) and/or critically located (<3 mm from critical structures) grade 1 intracranial meningiomas. The main aim was to evaluate the safety of hypo-RS in terms of absence of adverse events. The secondary aim was to evaluate tumor response in terms of local control, defined as stability or reduction of lesion volume.

Methods and Materials: We prospectively enrolled patients with diagnoses of grade 1 meningiomas, large size and/or critically located lesions, either histologically diagnosed or imaging defined. Additional inclusion criteria were signed informed consent, an age of ≥18 years, and Karnofsky Performance Status ≥70.

Results: Between 2011 and 2016, 178 patients were consecutively enrolled. The median follow-up was 53 months (range, 4-101 months). Overall, the toxicity rate was 12.7% (21 of 166 patients). At a 5-year minimum follow-up, the patients' toxicity rates were 11.7 % (9 of 77 patients). Symptom evaluation at both 3-year and last follow-up showed an improvement in most of the patients. Five-year local tumor control was 97% (95% confidence interval, 92%-99%).

Conclusions: Hypo-RS schedule of 25 Gy in 5 fractions is a well-tolerated option in the treatment of large-volume and/or critically located benign meningiomas. Early results suggest favorable local control, although longer-term follow-up is needed.

- Neurologic status at baseline showed that 50 (30%) patients did not have any neurologic symptoms and 116 (70%) patients presented 1 or more cranial nerve dysfunctions, including

  trigeminal pain/paresthesia (25%),

  visual impairment

  (44%) and

  facial nerve dysfunction

  (13%)

As regards III/IV/VI cranial nerves, 1 patient (2%)reported a worsening in preexisting deficits while 27 (55%)patients showed an improvement at last follow-up.
Visual acuity (II cranial nerve) was stable in 87% of patients; 5% reported a worsening (3 patients with preexisting grade 3 visual impairment had grade 4 visual deterioration) and 8% of patients showed an improvement at last follow-up.
Furthermore, we evaluated dosimetric data of patients who developed visual toxicity and compared them with values of patients who did not. Compared with the 95th percentile of maximum dose chiasm or optic nerve of patients who did not show visual toxicity, only 1 patient developing visual toxicity had a higher value (29.7 Gy as punctual dose delivered to a volume <0.5 cm3)

Brain metastases

Practical Radiation Oncology® (2022) 12, 265–282

www.practicalradonc.org

Clinical Practice Guideline

Radiation Therapy for Brain Metastases: An ASTRO Clinical Practice Guideline

Vinai Gondi, MD,[a,*] Glenn Bauman, MD,[b] Lisa Bradfield, BA.[c]

Resected metastases

Table 4 Indications for observation, postoperative SRS, WBRT, or preoperative SRS

KQ2 Recommendations	Strength of Recommendation	Quality of Evidence (refs)
1. For patients with resected brain metastases, radiation therapy (SRS or WBRT) is recommended to improve intracranial disease control.	Strong	High 13,50,51
2. For patients with resected brain metastases and limited additional brain metastases, SRS is recommended over WBRT to preserve neurocognitive function and patient-reported QoL.	Strong	Moderate 52
3. For patients whose brain metastasis is planned for resection, preoperative SRS is conditionally recommended as a potential alternative to postoperative SRS.	Conditional	Low 53,54

Abbreviations: KQ = key question; QoL = quality of life; SRS = stereotactic radiosurgery; WBRT = whole brain radiation therapy.

Table 5 Recommended postoperative cavity single-fraction SRS dosing guidance[52]

Cavity volume (cm^3)*	Single-fraction SRS dose (cGy)
<4.2 cm^3	2000 cGy
≥4.2 to <8.0 cm^3	1800 cGy
≥8.0 to <14.4 cm^3	1700 cGy
≥14.4 to <20.0 cm^3	1500 cGy
≥20.0 to <30.0 cm^3	1400 cGy
≥30.0 cm^3 to <5.0 cm max	1200 cGy

Abbreviation: SRS = stereotactic radiosurgery.
* Given the irregular shape of surgical cavities, the total prescribed dose should be based on the surgical cavity volume with a maximum cross-sectional diameter of <5.0 cm.

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International Journal of Radiation Oncology*Biology*Physics

Volume 114, Issue 3, Supplement, 1 November 2022, Pages S9-S10

Part of special issue:

ASTRO Annual 2022 Meeting

108

Risk Factors for Progression and Toxicity after Preoperative Radiosurgery for Resected Brain Metastases: A PROPS-BM Multicenter Cohort Study

R.S. Prabhu [1], T. Akinyelu [2], Z.K. Vaslow [3], J.K. Matsui [4], T. Dan [5], M.V. Mishra [6], E.S. Murphy [7], S. Boyles [8], H.K. Perlow [9], J.D. Palmer [9], T. Patel [10], Z. Wardak [11], G.F. Woodworth [12], A. Ksendzovsky [13], K. Yang [14], S.T. Chao [15]

Purpose/Objective(s)

Preoperative (preop) stereotactic radiosurgery (SRS) is a feasible alternative to postoperative (postop) SRS with potential benefits in adverse radiation effect (ARE) and meningeal disease (MD) compared to postop SRS. The goal of this study was to determine risk factors for progression and toxicity after preop SRS in an expanded multicenter cohort.

Local recurrence at 2 years 14.5 %

Radiotherapy and Oncology
Volume 142, January 2020, Pages 27-35

Systematic Review

Post-operative stereotactic radiosurgery following excision of brain metastases: A systematic review and meta-analysis

NB

radiation necrosis with post op SRS 7 %

LC rate at 1 year 84 %

MD risk 12.5 %

The cohort consisted of 378 patients with 389 preop SRS treated index lesions. Most patients (61.1%) had a single BM, underwent gross total resection (GTR, 95.4%), and had non-small cell lung (NSCLC, 47.9%), breast (16.1%), or melanoma (11.4%) cancer. Median dose was 15 Gy in 1 fraction to a median gross tumor volume (GTV) of 10.1 cc. Median interval between preop SRS and surgery was 2 days. Median cranial imaging follow-up interval was 9.5 months overall and 17.5 months for alive patients. The 2-year cavity local recurrence (LR) rate was 14.5%. Multivariable analysis (MVA) for LR demonstrated subtotal resection (STR, vs. GTR), single fraction SRS (vs. fractionated), larger GTV, gastrointestinal (GI) primary (vs. NSCLC), active systemic disease, and piecemeal resection (vs. en bloc) to be associated with higher risk of LR. Of note, interval between preop SRS and surgery was not significant. The 2-year any grade ARE rate was 7.7%. MVA for ARE demonstrated only larger planning target volume (PTV) margin expansion as associated with higher risk of ARE. The 2-year rate of MD was 5.6%. Most MD (76%) was classical type, with the remainder being nodular type. MVA for MD demonstrated STR (vs. GTR) and breast or melanoma histology (vs. NSCLC) as associated with higher risk of MD. Of note, posterior fossa location and type of surgical resection were not significant.

ASCO special articles

Treatment for Brain Metastases: ASCO-SNO-ASTRO Guideline

Michael A. Vogelbaum, MD, PhD[1]; Paul D. Brown, MD[2]; Hans Messersmith, MPH[3]; Priscilla K. Brastianos, MD[4]; Stuart Burri, MD[5]; Dan Cahill, MD, PhD[4]; Ian F. Dunn, MD[6]; Laurie E. Gaspar, MD, MBA[7,8]; Na Tosha N. Gatson, MD, PhD[9,10]; Vinai Gondi, MD[11]; Justin T. Jordan, MD[4]; Andrew B. Lassman, MD[12]; Julia Maues, MA[13]; Nimish Mohile, MD[14]; Navid Redjal, MD[15]; Glen Stevens, DO, PhD[16]; Erik Sulman, MD, PhD[17]; Martin van den Bent, MD[18]; H. James Wallace, MD[19]; Jeffrey S. Weinberg, MD[20]; Gelareh Zadeh, MD, PhD[21]; and David Schiff, MD[22]

Recommendation 2.1. Patients with symptomatic brain metastases should be offered local therapy (radiosurgery and/or 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).

RECOMMENDATIONS Surgery is a reasonable option for patients with brain metastases. Patients with large tumors with mass effect are more likely to benefit than those with multiple brain metastases and/or uncontrolled systemic disease. Patients with symptomatic brain metastases should receive local therapy regardless of the systemic therapy used. For patients with asymptomatic brain metastases, local therapy should not be deferred unless deferral is specifically recommended in this guideline. The decision to defer local therapy should be based on a multidisciplinary discussion of the potential benefits and harms that the patient may experience. Several regimens were recommended for non–small-cell lung cancer, breast cancer, and melanoma. For patients with asymptomatic brain metastases and no systemic therapy options, stereotactic radiosurgery (SRS) alone should be offered to patients with one to four unresected brain metastases, excluding small-cell lung carcinoma. SRS alone to the surgical cavity should be offered to patients with one to two resected brain metastases. SRS, whole brain radiation therapy, or their combination are reasonable options for other patients. Memantine and hippocampal avoidance should be offered to patients who receive whole brain radiation therapy and have no hippocampal lesions and 4 months or more expected survival. Patients with asymptomatic brain metastases with either Karnofsky Performance Status ≤ 50 or Karnofsky Performance Status < 70 with no systemic therapy options do not derive benefit from radiation therapy.

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).

Qualifying Statement: The expert panel recognizes that as of this publication, icotinib is not approved by the US Food and Drug Administration or the European Medicines Agency.

Recommendation 2.4. Alectinib, brigatinib, or ceritinib may be offered to patients with asymptomatic brain metastases from *ALK*-rearranged 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).

Recommendation 2.5. Pembrolizumab may be offered to patients with asymptomatic brain metastases from immunotherapy-naïve, programmed death-ligand 1–NSCLC who are also receiving pemetrexed and a platinum agent (Type: informal consensus; 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).

Recommendation 2.7. The combination of tucatinib, trastuzumab, and capecitabine may be offered to patients with human epidermal growth factor receptor 2–positive metastatic breast cancer who have asymptomatic brain metastases and have progressed on previous trastuzumab, pertuzumab, and/or trastuzumab emtansine–based therapy. If these agents are used, local therapy may be delayed until there is evidence of intracranial progression (Type: evidence-based; Evidence quality: low; Strength of recommendation: weak).

Recommendation 3.1. Radiation therapy should not be offered to patients with asymptomatic brain metastases who have:
- Performance status Karnofsky Performance Status (KPS) ≤ 50 or less, *or*
- Performance status KPS < 70 and no systemic therapy options (Type: evidence-based; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 3.2. SRS alone (as opposed to WBRT or combination of WBRT and SRS) should be offered to patients with one to four unresected brain metastases, excluding small-cell carcinoma.

ASCO special articles

Treatment for Brain Metastases: ASCO-SNO-ASTRO Guideline

Michael A. Vogelbaum, MD, PhD[1]; Paul D. Brown, MD[2]; Hans Messersmith, MPH[3]; Priscilla K. Brastianos, MD[4]; Stuart Burri, MD[5]; Dan Cahill, MD, PhD[6]; Ian F. Dunn, MD[6]; Laurie E. Gaspar, MD, MBA[7,8]; Na Tosha N. Gatson, MD, PhD[9,10]; Vinai Gondi, MD[11]; Justin T. Jordan, MD[4]; Andrew B. Lassman, MD[12]; Julia Maues, MA[13]; Nimish Mohile, MD[14]; Navid Redjal, MD[15]; Glen Stevens, DO, PhD[16]; Erik Sulman, MD, PhD[17]; Martin van den Bent, MD[18]; H. James Wallace, MD[19]; Jeffrey S. Weinberg, MD[20]; Gelareh Zadeh, MD, PhD[21]; and David Schiff, MD[22]

Multidisciplinary assessment and patient-centered decision making are essential to optimally select patients in whom local therapy for brain metastases may be safely and appropriately delayed

For patients with symptomatic brain metastases who are candidates for immunotherapy or CNS-active targeted therapy, based on eligibility and clinical context, upfront local therapy (radiation and/or surgery) is recommended because studies of immunotherapy and CNS-active targeted therapy have demonstrated limited response rates and/or limited durability of radiographic stability

Prospective studies are ongoing (NCT03340129, NCT02858869, NCT02978404) and more are needed to assess the optimal combination of local therapy with the evolving landscape of systemic therapies to maximize CNS-tumor control and patient survival.

Annals of Oncology
Volume 33, Issue 3, March 2022, Pages 321-329

Original Article

Tucatinib versus placebo added to trastuzumab and capecitabine for patients with pretreated HER2+ metastatic breast cancer with and without brain metastases (HER2CLIMB): final overall survival analysis

G. Curigliano [1], V. Mueller [2], V. Borges [3], E. Hamilton [4], S. Hurvitz [5], S. Loi [6], R. Murthy [7], A. Okines [8], E. Paplomata [9,†], D. Cameron [10], L.A. Carey [11], K. Gelmon [12], G.N. Hortobagyi [7], I. Krop [13], S. Loibl [14], M. Pegram [15], D. Slamon [5], J. Ramos [16], W. Feng [16], E. Winer [13]

Highlights

- Tucatinib combination shows continued prolongation of overall survival in patients with HER2+ metastatic breast cancer.
- Overall survival benefit was consistent across all prespecified subgroups, including patients with brain metastases.
- The tucatinib combination was well tolerated with a low rate of discontinuation due to adverse events (5.9%).

Research

JAMA Oncology | Original Investigation

Tucatinib vs Placebo, Both in Combination With Trastuzumab and Capecitabine, for Previously Treated ERBB2 (HER2)-Positive Metastatic Breast Cancer in Patients With Brain Metastases

Updated Exploratory Analysis of the HER2CLIMB Randomized Clinical Trial

…helot, MD, PhD; Philippe L. Bedard, MD; …liano, MD, PhD; Michael P. DiGiovanna, MD, PhD; …D; Sibylle Loibl, MD, PhD; …non, MD;

Key Points

Question Can tucatinib, trastuzumab, and capecitabine provide systemic and intracranial benefit for patients with ERBB2 (HER2)-positive metastatic breast cancer and brain metastases?

Findings In this exploratory subgroup analysis of a randomized clinical trial of 612 patients with ERBB2-positive breast cancer, overall survival, intracranial efficacy, and new brain lesion–free survival were evaluated. Tucatinib in combination with trastuzumab and capecitabine prolonged median overall survival by 9.1 months in patients with brain metastases and reduced the risk of developing new brain lesions as sites of first progression or death by 45.1% in all patients.

Meaning Findings suggest tucatinib in combination with trastuzumab and capecitabine provides survival benefits and delays development of new brain lesions, representing an important treatment option for patients with ERBB2-positive metastatic breast cancer, including those with brain metastases.

Table. Confirmed Intracranial Responses in Patients With Active Brain Metastases and Measurable Intracranial Lesions at Baseline

Intracranial response	Tucatinib combination (n = 55)[a]	Placebo combination (n = 20)[b]
Patients with objective response of confirmed complete response or partial response, No.	26	4
Confirmed ORR-IC, % (95% CI)	47.3 (33.7-61.2)	20.0 (5.7-43.7)
DOR-IC, median (95% CI), mo[c]	8.6 (5.5-10.3)	3.0 (3.0-10.3)

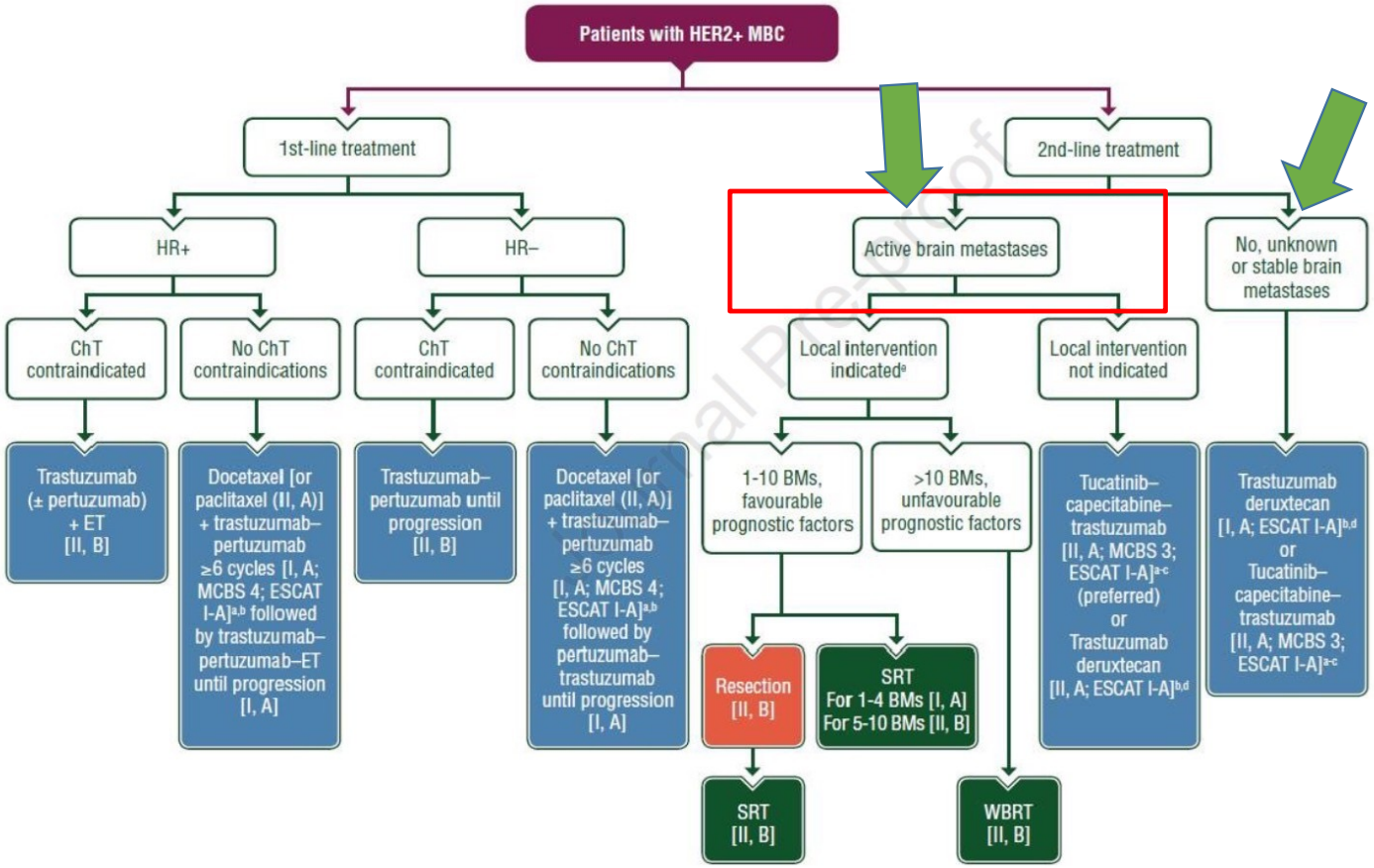
Abbreviations: DOR-IC, duration of intracranial response; ORR-IC, intracranial objective response rate.

[a] Tucatinib, trastuzumab, and capecitabine.

[b] Placebo, trastuzumab, and capecitabine.

[c] Calculated with the complementary log-log transformation method.

How The New Drugs Change the Algoritms
The Last Two Years Most Therapeutic Improvements in HER2 + Tumors



Gennari et al ESMO Guideline 2022

asco special articles

Treatment for Brain Metastases: ASCO-SNO-ASTRO Guideline

Michael A. Vogelbaum, MD, PhD[1]; Paul D. Brown, MD[2]; Hans Messersmith, MPH[3]; Priscilla K. Brastianos, MD[4]; Stuart Burri, MD[5]; Dan Cahill, MD, PhD[6]; Ian F. Dunn, MD[6]; Laurie E. Gaspar, MD, MBA[7,8]; Na Tosha N. Gatson, MD, PhD[9,10]; Vinai Gondi, MD[11]; Justin T. Jordan, MD[4]; Andrew B. Lassman, MD[12]; Julia Maues, MA[13]; Nimish Mohile, MD[14]; Navid Redjal, MD[15]; Glen Stevens, DO, PhD[16]; Erik Sulman, MD, PhD[17]; Martin van den Bent, MD[18]; H. James Wallace, MD[19]; Jeffrey S. Weinberg, MD[20]; Gelareh Zadeh, MD, PhD[21]; and David Schiff, MD[22]

Table 7 Risks of symptomatic radionecrosis with WBRT and/or SRS

KQ4 Recommendation	Strength of Recommendation	Quality of Evidence (refs)
1. For patients with brain metastases, limiting the single-fraction V_{12Gy} to brain tissue (normal brain *plus* target volumes) to $\leq$10 cm^3 is conditionally recommended. Implementation remark: Any brain metastasis with an associated tissue V_{12Gy} >10 cm^3 may be considered for fractionated SRS to reduce risk of radionecrosis (see KQ1).	Conditional	Low 12,88

Abbreviations: KQ = key question; SRS = stereotactic radiosurgery; WBRT = whole brain radiation therapy.

Quantitative Analysis of Normal Tissue Effect in the Clinic (QUANTEC) recommendation to limit single-fraction V12Gy to 5 to 10 cm3 remains prudent
For patients treated with 5-fraction fractionated SRS, these studies suggest keeping the V30Gy of normal brain (total brain minus target volume) to <10.5 cm3

Although reports are limited and quality of evidence is mixed, there may be combinations of certain systemic therapy agents (TKIs, T-DM1) and SRS that are associated with a higher risk of radionecrosis (30%-40%) than those reported with SRS alone (Zhuang 2020 ,Soliman 2020). With respect to combinations of immune checkpoint inhibitors with SRS, reports are also mixed, some showing a higher incidence of radionecrosis with combination therapy. However, there are also several reports showing that the incidence of radionecrosis is low with combination of immune checkpoint inhibition and SRS and similar to rates reported for SRS alone.

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EDITORIAL

The Art of Radiation Therapy: The Necessary Risk of Radiation Necrosis for Durable Control of Brain Metastases

Michael T. Milano, MD, PhD,* Scott G. Soltys, MD,† Lawrence B. Marks, MD,‡ Dwight E. Heron, MD,§ Ellen Yorke, PhD,‖ Jimm Grimm, PhD,¶ Andrew Jackson, PhD,‖ Alina Mihai, MD,# Robert D. Timmerman, MD,** Jinyu Xue, PhD,†† Brian D. Kavanagh, MD,‡‡ and Kristin J. Redmond, MD§§

Although such an approach of minimizing event rates can be attempted from HyTEC data, we suggest prescribing doses for intact brain metastases that are supported by published studies11,12 and corroborated by HyTEC, which analyzed TCP for “small,” “medium,” and “large” brain metastases (with diameters ≤2 cm, 2.1-3.0 cm, and 3.1-4.0 cm, respectively). From the HyTEC analyses, doses of 18 to 24 Gy £ 1, 9 to 10 Gy £ 3, or 6 to 7 Gy £ 5 led to TCP rates >70% to 95% (depending on tumor size and dose); the authors recommended consideration of fractionation for lesions >2 cm in size as a potential means to increase TCP and reduce NTCP. We suggest considering lower prescribed doses if predicted risks of symptomatic necrosis in an eloquent area are relatively high (eg, >20%-30%), even with fractionation, and if lower doses would plausibly markedly mitigate these risks without meaningfully compromising TCP. But again, the appropriateness of this strategy depends on the clinical situation, and we acknowledge that data (on which HyTEC based its analyses) needed to make these difficult decisions are lacking

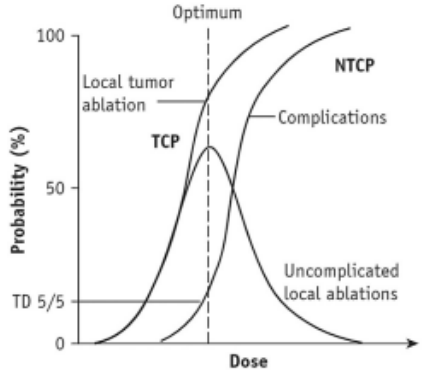

Fig. 1. Tumor control probability (TCP) and normal tissue complication probability (NTCP) as a function of dose.[5] The curves are presented in a generic manner to describe a concept of balancing risks and benefits. In applying this concept to brain metastases treated with stereotactic radiosurgery, the x-axis (dose) has different meanings TCP and NTCP. For TCP, dose is meant to imply prescribed dose, conceding that how one prescribes dose varies in clinical practice. For NTCP, an increased dose would increase the volume of brain or normal tissue receiving a given dose, which is the typical metric used in quantifying risks of necrosis (as described in the text). This exposure is dependent not only on prescribed dose and target size(s), but also planning margins, dose gradient, dose conformity and planning approaches. This simplified figure does not capture these nuances and merely demonstrates how balancing TCP and NTCP impact treatment decision-making. TD 5/5 = tolerance dose resulting in a 5% risk of toxicity at 5 years. *Abbreviations:* NTCP = normal tissue complication probability; TCP = tumor control probability.

Stereotactic radiosurgery versus whole brain radiotherapy in patients with intracranial metastatic disease and small-cell lung cancer: a systematic review and meta-analysis

Karolina Gaebe, Alyssa Y Li, Amy Park, Ambica Parmar, Benjamin H Lok, Arjun Sahgal, Kelvin K W Chan, Anders W Erickson, Sunit Das

Lancet Oncol 2022; 23: 931–39
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May 26, 2022
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Summary

Background Patients with small-cell lung cancer (SCLC) are at high risk for intracranial metastatic disease (IMD). Although stereotactic radiosurgery (SRS) has supplanted whole brain radiotherapy (WBRT) as first-line treatment for IMD in most solid cancers, WBRT remains first-line treatment for IMD in patients with SCLC. We aimed to evaluate the efficacy of SRS in comparison with WBRT and assess treatment outcomes following SRS.

Methods In this systematic review and meta-analysis, we searched MEDLINE, Embase, CENTRAL, and grey literature sources for controlled trials and cohort studies published in English reporting on SRS for IMD treatment in patients with SCLC from inception to March 23, 2022. Studies were excluded that did not report on SRS for IMD secondary to SCLC. Summary data were extracted. The primary outcome was overall survival, presented as pooled hazard ratios (HR) through random-effects meta-analysis for studies comparing SRS with WBRT with or without SRS boost, and as medians for single-arm SRS studies. This study is registered with the Open Science Framework, DOI 10.17605/OSF.IO/8M4HC, and PROSPERO, CRD42021258197.

Findings Of 3823 identified records, 31 were eligible for inclusion; seven were included in the meta-analysis. Overall survival following SRS was longer than following WBRT with or without SRS boost (HR 0·85; 95% CI 0·75–0·97; n=7 studies; n=18 130 patients), or WBRT alone (0·77; 0·72–0·83; n=7 studies; n=16 961 patients), but not WBRT plus SRS boost (1·17, 0·78–1·75; n=4 studies; n=1167 patients). Using single-arm studies, pooled median overall survival from SRS was 8·99 months (95% CI 7·86–10·16; n=14 studies; n=1682 patients). Between-study heterogeneity was considerable when pooled among all comparative studies (I^2=71·9%).

Interpretation These results suggest survival outcomes are equitable following treatment with SRS compared with WBRT in patients with SCLC and IMD. Future prospective studies should focus on tumour burden and differences in local and distant intracranial progression between WBRT-treated and SRS-treated patients with SCLC.

In the meantime, the repeated report of equitable overall survival, high intracranial control rates, and the convenient possibility of repeated SRS with single or few sessions might be reason enough to offer SRS instead of WBRT to selected patients with limited brain metastases from SCLC.

The ENCEPHALON trial is investigating the potential cognitive benefit of SRS versus WBRT in patients with SCLC,
and is expected to add substantial knowledge in the near future.

Spine tumors

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Guidelines

ESTRO ACROP guidelines for external beam radiotherapy of patients with complicated bone metastases

Eva Oldenburger [a,1], Stephanie Brown [b,1], Jonas Willmann [c], Joanne M. van der Velden [d,e], Mateu
Yvette M. van der Linden [d,e], Joanna Kazmierska [g,h], Johan Menten [a,i], Nicolaus Andratschke [c,2],
Peter Hoskin [b,j,*,2]

Box 1 Key recommendations: Classification of bone metastases

- Bone metastases – irrespective of size – should be regarded as uncomplicated if they are 1) painful; 2) without impending or existing pathologic fracture; and 3) without spinal cord or cauda equina compression, irrespective of size.
- Oligometastatic disease refers to a limited number of metastases and should be classified using the ESTRO-EORTC consensus classification.

No place for SRT out side clinical trials

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Radiotherapy and Oncology

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Guidelines

ESTRO ACROP guidelines for external beam radiotherapy of patients with uncomplicated bone metastases

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Critical Review

Stereotactic Radiosurgery for Postoperative Spine Malignancy: A Systematic Review and International Stereotactic Radiosurgery Society Practice Guidelines

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Abstract

Purpose: To determine safety and efficacy of postoperative spine stereotactic body radiation therapy (SBRT) in the published literature, and to present practice recommendations on behalf of the International Stereotactic Radiosurgery Society.

Methods and Materials: A systematic review of the literature was performed, specific to postoperative spine SBRT, using PubMed and Embase databases. A meta-analysis for 1-year local control (LC), overall survival (OS), and vertebral compression fracture probability was conducted.

Results: The literature search revealed 251 potentially relevant articles after duplicates were removed. Of these 56 were reviewed in-depth for eligibility and 12 met all the inclusion criteria for analysis. 7 studies were retrospective, 2 prospective observational and 3 were prospective phase 1 and 2 clinical trials. Outcomes for a total of 461 patients and 499 spinal segments were reported. Ten studies used a magnetic resonance imaging (MRI) scan fused to computed tomography (CT) simulation for treatment planning, and 2 investigations reported on all patients receiving a CT-myelogram at the time of planning. Meta-analysis for 1 year LC and OS was 88.9% and 57%, respectively. The crude reported vertebral compression fracture rate was 5.6%. One case of myelopathy was described in a patient with a previously irradiated spinal segment. One patient developed an esophageal fistula requiring surgical repair.

Conclusions: Postoperative spine SBRT delivers a high 1-year LC with acceptably low toxicity. Patients who may benefit from this include those with oligometastatic disease, radioresistant histology, paraspinal masses, or those with a history of prior irradiation to the affected spinal segment. The International Stereotactic Radiosurgery Society recommends a minimum interval of 8 to 14 days after invasive surgery before simulation for SBRT, with initiation of radiation therapy within 4 weeks of surgery. An MRI fused to the planning CT, or the use of a CT-myelogram, are necessary for target and organ-at-risk delineation. A planning organ-at-risk volume (PRV) of 1.5 to 2 mm for the spinal cord is advised.

Table 4 ISRS recommendations for the use of postoperative spine SBRT

Key recommendations
Patient selection
- Patients with oligometastatic disease.
- Patients with radioresistant histologies and/or those with mass-type tumors with paraspinal extension.
- If prior cEBRT or SBRT has been given to the affected spinal segment then salvage postoperative SBRT can be considered.
Treatment planning
- All patients should undergo an axial high-resolution 1.5 Tesla T1/T2 MRI of the affected spinal segment including at least one vertebral segment above and below the target volume for both target and OAR delineation. This MRI is fused to the planning CT scan. Use of gadolinium or CT contrast can assist in delineation of soft tissue tumor extension. A CT-myelogram can be considered, especially for cases where hardware artifact obscures canal on the MRI scan. In this scenario it is best to perform a simulation CT myelogram as opposed to a diagnostic CT myelogram that is then fused to the radiation planning CT.
- A 1.5-2 mm PRV should be applied to the spinal cord. The thecal sac does not need a PRV. Spinal cord and thecal sac dose limits vary based on fractionation. Published guidelines for dose constraints can be consulted as indicated.[34-36]
- The preoperative extent of epidural/paraspinal disease should be included in the postoperative CTV. This often requires the use of a "donut" type CTV.[38] A 5 mm superior/inferior CTV expansion including the spinal canal beyond visible epidural disease should also be considered, in addition to a 5 mm margin surrounding any paraspinal soft tissue disease extension while respecting anatomic boundaries. The surgical scar does not need to be included in the CTV. Contouring recommendations have been published by Chan et al and Redmond et al.[38,39]
- A minimum time interval of 1-week from the time of a minimally invasive spinal surgery, and 8-14 days for more invasive surgeries, should be maintained before simulation for SBRT. Delays longer than 4 weeks postoperatively to the initiation of radiation may result in worse tumor control.
Follow-up
- In addition to history and physical examination, a spine MRI should be considered every 2-3 months post-SBRT for the first year and then every 3-6 months thereafter.

Glial tumors

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Review

Adult type diffuse gliomas in the new 2021 WHO Classification

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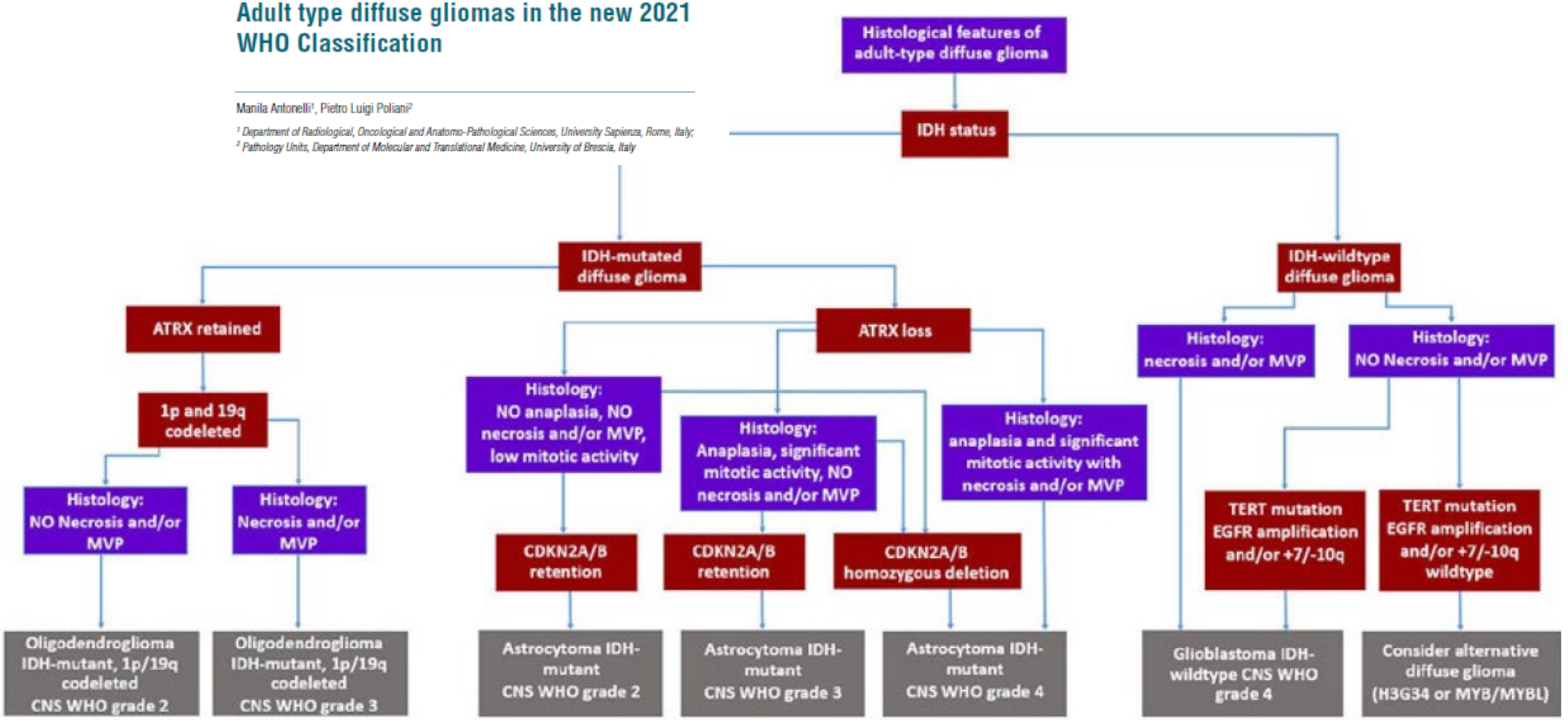

In all other cases of diffuse gliomas, a lack of IDH1-R132H immunoreactivity should be followed by IDH1 and IDH2 DNA sequencing

IDH-wildtype diffuse gliomas without vascular proliferation or necrosis should be tested for

EGFR amplification,

TERT promoter mutation and/or a +7/–10 cytogenetic

In addition, the presence of histone H3.3 G34R/V mutations should be evaluated to identify H3.3 G34-mutant diffuse hemispheric gliomas in young patients with IDH-wildtype gliomas and ATRX mutated neoplasm.

Diffuse gliomas of the thalamus, brainstem or spinal cord must be tested for histone H3K27M mutations to identify H3K27M-altered diffuse midline gliomas.

Finally, MYB- or MYBL1-altered or diffuse low-grade glioma MAPK pathway-altered should be considered in diffuse low grade IDH-wild type in adults

Neuro-Oncology Advances
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Brief Communication

TERT promotor status does not add prognostic information in IDH-wildtype glioblastomas fulfilling other diagnostic WHO criteria: A report of the RANO *resect* group

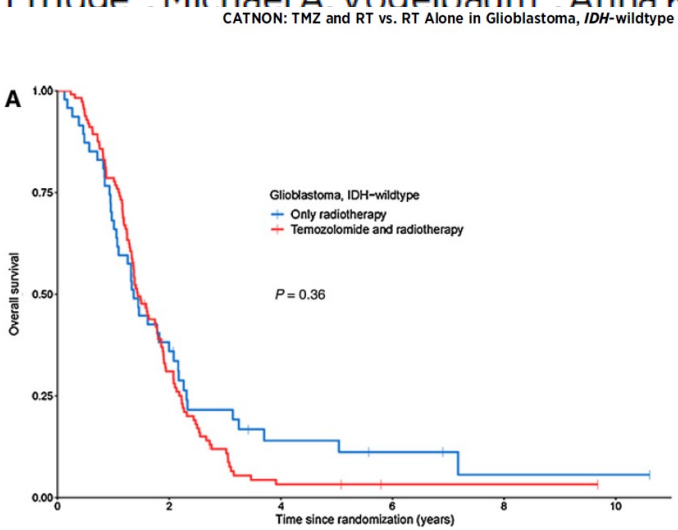
This means that is possible to define a molecular glioblastoma, IDH-wildtype CNS WHO grade 4, even in cases that otherwise appear histologically lower grade 2 o 3, when present concurrent gain of whole chromosome 7 and loss of whole chromosome 10 (+7/–10), EGFR amplification and/or TERT promoter mutation.

However, TERT promoter mutation is the less specific parameter for GBM than the aforementioned two parameters, suggesting being cautious to perform a diagnosis of molecular glioblastoma if only this alteration is present in otherwise low grade diffuse IDH wildtype glioma

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

Temozolomide and Radiotherapy versus Radiotherapy Alone in Patients with Glioblastoma, *IDH*-wildtype: *Post Hoc* Analysis of the EORTC Randomized Phase III CATNON Trial

C. Mircea S. Tesileanu[1], Marc Sanson[2], Wolfgang Wick[3], Alba A. Brandes[4], Paul M. Clement[5], Sara C. Erridge[6], Michael A. Vogelbaum[7], Anna K. Nowak[8,9,10], Jean-Francois Baurain[11], Warren P. Mason[12], Helen [illegible], Robert A [illegible], Robert [illegible], Iris de [illegible], Wilfred [illegible], Thierry [illegible]



Results: A total of 159 of these tumors met the WHO 2021 molecular criteria for glioblastoma,IDH-wt., 47 received radiotherapy only and 112 received a combination of radiotherapy and temozolomide. There was no added effect of temozolomide on either overall survival or progression-free survival . MGMT promoter methylation was prognostic for overall survival, but was not predictive for outcome to temozolomide treatment either with respect to overall survival or progression-free survival.

Conclusions: In this cohort of patients with glioblastoma, IDH-wt temozolomide treatment did not add benefit beyond that observed from radiotherapy, regardless of MGMT promoter status.

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Review Article

Executive summary of American Radium Society's appropriate use criteria for the postoperative management of lower grade gliomas

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Neuro-Oncology

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Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline

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Clinical Practice Guideline

Radiation Therapy for IDH-Mutant Grade 2 and Grade 3 Diffuse Glioma: An ASTRO Clinical Practice Guideline

Dabrafenib plus trametinib in patients with *BRAF*^{V600E}-mutant low-grade and high-grade glioma (ROAR): a multicentre, open-label, single-arm, phase 2, basket trial

Patrick Y Wen, Alexander Stein, Martin van den Bent, Jacques De Greve, Antje Wick, Filip Y F L de Vos, Nikolas von Bubnoff, Myra E van Linde, Albert Lai, Gerald W Prager, Mario Campone, Angelica Fasolo, Jose A Lopez-Martin, Tae Min Kim, Warren P Mason, Ralf-Dieter Hofheinz, Jean-Yves Blay, Daniel C Cho, Anas Gazzah, Damien Pouessel, Jeffrey Yachnin, Aislyn Boran, Paul Burgess, Palanichamy Ilankumaran, Eduard Gasal, Vivek Subbiah

Summary

Background Effective treatments are needed to improve outcomes for high-grade glioma and low-grade glioma. The activity and safety of dabrafenib plus trametinib were evaluated in adult patients with recurrent or progressive *BRAF*^{V600E} mutation-positive high-grade glioma and low-grade glioma.

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Published Online
November 24, 2021
https://doi.org/10.1016/

Interim analysis of 45 pts :
33% responders in HGG group (median FU 12 months)
69% responders in LGG group (median follow up 32 months)
53 % grade 3 toxicities (no neurological side effects)

- The BRAF inhibitor dabrafenib has shown meaningful clinical activity in paediatric patients with BRAF V600 mutation-positive low-grade glioma and high-grade glioma.
- Dual blockade of the MAPK pathway using dabrafenib and the MEK inhibitor trametinib has shown activity in multiple tumour types and is a standard of care in BRAF V600-mutant melanoma, non-small-cell lung cancer, and anaplastic thyroid cancer. Compared with BRAF inhibitor monotherapy, combined treatment showed superior outcomes with regard to progression-free survival and overall survival and reduced the incidence of skin-related toxicities in melanoma and non-small-cell lung cancer. Furthermore, there is emerging evidence that acquired resistance to BRAF inhibitor monotherapy develops in gliomas, as in other tumour types, which might be mitigated by dual inhibition
- Taken together, these data support the investigation of dabrafenib plus trametinib in adult patients with BRAFV ^{600}E mutation positive glioma.