

Radiation Therapy for Brain Metastases: ASCO Guideline Endorsement of ASTRO Guideline

David Schiff, MD¹; Hans Messersmith, MPH²; Priscilla K. Brastianos, MD³; Paul D. Brown, MD⁴; Stuart Burri, MD⁵; Ian F. Dunn, MD⁶; Laurie E. Gaspar, MD, MBA^{7,8}; Vinai Gondi, MD⁹; Justin T. Jordan, MD, MPH³; Julia Maues, MA¹⁰; Nimish Mohile, MD¹¹; Navid Redjal, MD¹²; Glen H.J. Stevens, DO, PhD¹³; Erik P. Sulman, MD, PhD¹⁴; Martin van den Bent, MD¹⁵; H. James Wallace, MD¹⁶; Gelareh Zadeh, MD, PhD¹⁷; and Michael A. Vogelbaum, MD, PhD¹⁸

PURPOSE American Society of Radiation Oncology (ASTRO) has developed a guideline on appropriate radiation therapy for brain metastases. ASCO has a policy and set of procedures for endorsing clinical practice guidelines that have been developed by other professional organizations.

METHODS “Radiation Therapy for Brain Metastases: An ASTRO Clinical Practice Guideline”² was reviewed for developmental rigor by methodologists. An ASCO Endorsement Panel subsequently reviewed the content and the recommendations.

RESULTS The ASCO Endorsement Panel determined that the recommendations from the ASTRO guideline, published May 6, 2022, are clear, thorough, and based upon the most relevant scientific evidence. ASCO endorses “Radiation Therapy for Brain Metastases: An ASTRO Clinical Practice Guideline.”²

RECOMMENDATIONS Within the guideline, stereotactic radiosurgery (SRS) is recommended for patients with Eastern Cooperative Oncology Group performance status of 0-2 and up to four intact brain metastases, and conditionally recommended for patients with up to 10 intact brain metastases. The guideline provides detailed dosing and fractionation recommendations on the basis of the size of the metastases. For patients with resected brain metastases, radiation therapy (SRS or whole-brain radiation therapy [WBRT]) is recommended to improve intracranial disease control; if there are limited additional brain metastases, SRS is recommended over WBRT. For patients with favorable prognosis and brain metastases ineligible for surgery and/or SRS, WBRT is recommended with hippocampal avoidance where possible and the addition of memantine is recommended. For patients with brain metastases, limiting the single-fraction V_{12Gy} to brain tissue to $\leq 10 \text{ cm}^3$ is conditionally recommended.

Additional information is available at www.asco.org/neurooncology-guidelines.

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ASSOCIATED CONTENT

Appendix

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

ASCO, the Society for Neuro-Oncology (SNO), and the American Society of Radiation Oncology (ASTRO) published a joint guideline on the treatment of brain metastases on December 21, 2021.¹ This guideline, referred to as the joint guideline in this endorsement, presented general recommendations on the use of radiation therapy for patients with brain metastases. However, ASTRO recognized a need for more detailed recommendations that would address specifics of dose, fractionation schedule, sequence of surgery and radiation, as well as radionecrosis (a topic not addressed in the joint guideline). To fulfill this need, ASTRO developed a radiation therapy for brain metastases guideline.² Because the joint guideline and

the ASTRO guideline were developed simultaneously with several common panel members, and to more widely disseminate and ideally increase the uptake and use of these important recommendations, the ASTRO guideline was a prime candidate for consideration of an ASCO endorsement.

OVERVIEW OF THE ASCO GUIDELINE ENDORSEMENT PROCESS

ASCO has policies and procedures for endorsing practice guidelines that have been developed by other professional organizations. The goal of guideline endorsement is to increase the number of high-quality, ASCO-vetted guidelines available to the ASCO membership. The ASCO endorsement process involves an

THE BOTTOM LINE

Radiation Therapy for Brain Metastases: ASCO Guideline Endorsement of ASTRO Guideline

ASCO endorses “Radiation Therapy for Brain Metastases: An ASTRO Clinical Practice Guideline.”²

Guideline Questions

KQ1: What are the indications for stereotactic radiosurgery (SRS) alone for patients with intact brain metastases?

KQ2: What are the indications for observation, preoperative SRS, or postoperative SRS or whole-brain radiation therapy (WBRT) in patients with resected brain metastases?

KQ3: What are the indications for WBRT for patients with intact brain metastases?

KQ4: What are the risks of symptomatic radionecrosis with WBRT and/or SRS for patients with brain metastases?

Target Population

Patients with brain metastases.

Target Audience

Radiation oncologists, neurosurgeons, medical physicists, clinicians working in multidisciplinary care, and patients with brain metastases.

Methods

An ASCO Expert Panel was convened to consider endorsing the American Society of Radiation Oncology (ASTRO) Radiation Therapy for Brain Metastases recommendations that were based on a systematic review of the medical literature. The ASCO Expert Panel considered the methodology employed in the ASTRO guideline by considering the results from the AGREE II review instrument. The ASCO Expert Panel carefully reviewed the ASTRO guideline content to determine appropriateness for ASCO endorsement.

Recommendations

These research questions and recommendations are reprinted from the ASTRO guideline. The ASTRO evidence quality and strength of recommendation definitions are described in Appendix [Table A2](#) (online only).

Recommendation KQ1.1. For patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 and up to four intact brain metastases, SRS is recommended (evidence quality: high; strength of recommendation: strong).

Recommendation KQ1.2. For patients with an ECOG performance status of 0-2 and 5-10 intact brain metastases, SRS is conditionally recommended (evidence quality: low; strength of recommendation: conditional).

Recommendation KQ1.3. For patients with intact brain metastases measuring < 2 cm in diameter, single-fraction SRS with a dose of 2,000-2,400 cGy is recommended (evidence quality: moderate; strength of recommendation: strong).

Implementation remark

If multifraction SRS were chosen (eg, $V_{12Gy} > 10 \text{ cm}^3$ [see KQ4]), options include 2,700 cGy in three fractions or 3,000 cGy in five fractions.

Recommendation KQ1.4. For patients with intact brain metastases measuring ≥ 2 cm to < 3 cm in diameter, single-fraction SRS using 1800 cGy or multifraction SRS (eg, 2,700 cGy in three fractions or 3,000 cGy in five fractions) is conditionally recommended (see KQ4; evidence quality: low; strength of recommendation: conditional).

Recommendation KQ1.5. For patients with intact brain metastases measuring ≥ 3 cm to 4 cm in diameter, multifraction SRS (eg, 2,700 cGy in three fractions or 3,000 cGy in five fractions) is conditionally recommended (evidence quality: low; strength of recommendation: conditional).

Implementation remarks

- If single-fraction SRS were chosen, doses up to 1,500 cGy may be used (see KQ4).
- Multidisciplinary discussion with neurosurgery to consider surgical resection is suggested for all tumors causing mass effect, irrespective of tumor size.

Recommendation KQ1.6. For patients with intact brain metastases measuring > 4 cm in diameter, surgery is conditionally recommended, and if not feasible, multifraction SRS is preferred over single-fraction SRS (evidence quality: low; strength of recommendation: conditional).

Implementation remark

Given limited evidence, SRS for tumor size > 6 cm is discouraged.

Recommendation KQ1.7. For patients with symptomatic brain metastases who are candidates for local therapy and CNS-active systemic therapy, upfront local therapy is recommended (evidence quality: low; strength of recommendation: strong).

(continued on following page)

THE BOTTOM LINE (CONTINUED)

Recommendation KQ1.8. For patients with asymptomatic brain metastases eligible for CNS-active systemic therapy, multi-disciplinary and patient-centered decision making is conditionally recommended to determine whether local therapy may be safely deferred (evidence quality: expert opinion; strength of recommendation: conditional).

Implementation remark

The decision to defer local therapy should consider factors such as brain metastasis size, parenchymal brain location, number of metastases, likelihood of response to specific systemic therapy, access to close neuro-oncologic surveillance, and availability of salvage therapies.

Recommendation KQ2.1. For patients with resected brain metastases, radiation therapy (SRS or WBRT) is recommended to improve intracranial disease control (evidence quality: high; strength of recommendation: strong).

Recommendation KQ2.2. For patients with resected brain metastases and limited additional brain metastases, SRS is recommended over WBRT to preserve neurocognitive function and patient-reported quality of life (QoL; evidence quality: moderate; strength of recommendation: strong).

Recommendation KQ2.3. For patients whose brain metastasis is planned for resection, preoperative SRS is conditionally recommended as a potential alternative to postoperative SRS (evidence quality: low; strength of recommendation: conditional).

Recommendation KQ3.1. For patients with favorable prognosis (estimated using a validated brain metastases prognostic index) and brain metastases ineligible for surgery and/or SRS, WBRT (eg, 3,000 cGy in 10 fractions) is recommended as primary treatment (see KQ1, recommendations 7 and 8 for consideration of systemic therapy; evidence quality: high; strength of recommendation: strong).

Recommendation KQ3.2. For patients with favorable prognosis and brain metastases receiving WBRT, hippocampal avoidance is recommended (evidence quality: high; strength of recommendation: strong).

Implementation remark

Hippocampal avoidance is not appropriate in cases of brain metastases in close proximity to the hippocampi or in cases of leptomeningeal disease.

Recommendation KQ3.3. For patients with favorable prognosis and brain metastases receiving WBRT or hippocampal-avoidance WBRT, addition of memantine is recommended (evidence quality: low; strength of recommendation: strong).

Recommendation KQ3.4. For patients with favorable prognosis and limited brain metastases, routine adjuvant WBRT added to SRS is not recommended (evidence quality: high; strength of recommendation: strong).

Implementation remark

To maximize intracranial control and/or when close imaging surveillance with additional salvage therapy is not feasible, adjuvant WBRT may be offered in addition to SRS.

Recommendation KQ3.5. For patients with poor prognosis and brain metastases, early introduction of palliative care for symptom management and caregiver support are recommended (evidence quality: moderate; strength of recommendation: strong).

Implementation remarks

- Supportive care only (with omission of WBRT) should be considered.
- If WBRT is used, brief schedules (eg, five fractions) are preferred.

Recommendation KQ4.1. For patients with brain metastases, limiting the single-fraction V_{12Gy} to brain tissue (normal brain plus target volumes) to $\leq 10 \text{ cm}^3$ is conditionally recommended (evidence quality: low; strength of recommendation: conditional).

Implementation remark

Any brain metastasis with an associated tissue $V_{12Gy} > 10 \text{ cm}^3$ may be considered for fractionated SRS to reduce risk of radionecrosis (see KQ1).

Additional Resources

More information, including a supplement, slide sets, and clinical tools and resources, is available at www.asco.org/neurooncology-guidelines. The Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the methods used to develop this guideline. Patient information is available at www.cancer.net.

A link to “Radiation Therapy for Brain Metastases: An ASTRO Clinical Practice Guideline” can be found at <https://www.astro.org/Patient-Care-and-Research/Clinical-Practice-Statements>

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

assessment by ASCO staff of candidate guidelines for methodological quality using the Rigor of Development subscale of the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument (see the Data Supplement [online only] for more details).

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Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with ASCO’s Conflict of Interest Policy Implementation for Clinical Practice Guidelines (“Policy,” found at <http://www.asco.org/guideline-methodology>). All members of the Expert Panel completed ASCO’s disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or

commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker’s bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

CLINICAL QUESTION(S) AND TARGET POPULATION

The ASTRO guideline addressed the key questions (KQ) reprinted in [Table 1](#).

SUMMARY OF THE ASTRO GUIDELINE DEVELOPMENT METHODOLOGY

The ASTRO guideline was developed by a task force that included experts in radiation and medical oncology in accordance with the ASTRO Clinical Practice Guideline Methodology Guide.³ It is based on a systematic review conducted by the Agency for Healthcare Research and Quality (AHRQ)⁴ as well as an ASTRO supplemental systematic review that covers the available evidence published as late as September 2020. Full details of this systematic review and the identified evidence can be found in the guideline and in the separate AHRQ report.

RESULTS OF THE ASCO METHODOLOGY REVIEW

An initial methodology evaluation of the ASTRO guideline was completed independently for each guideline in the series by two ASCO guideline staff members using the Rigor of Development subscale from the AGREE II instrument.⁵ The details of the scores are available in Data Supplement 2; the guideline achieved an overall Rigor of Development score of 95%. The preliminary ASCO content reviewer of the guideline (Data Supplement 1), as well as the ASCO Expert Panel, found the recommendations well supported in the original guideline. Each section, including an introduction, was clear and well referenced from the systematic review. This is the most recent information as of the publication date.

As this ASTRO guideline has a very recent systematic review (as of September 2020) and as the recently published ASCO-SNO-ASTRO joint guideline on the treatment of brain metastases also has a recent review (August 2020) as an independent check on the evidence, no additional systematic review was conducted by ASCO for this endorsement.

RESULTS OF THE ASCO CONTENT REVIEW

The ASCO Expert Panel reviewed the ASTRO guideline and concurs that the recommendations are clear, thorough, based on the most relevant scientific evidence in this content area, and present options that will be acceptable to patients. Overall, the ASCO Expert Panel agrees with the recommendations as stated in the guideline. The

TABLE 1. ASTRO Guideline Questions

KQ	Population	Intervention	Comparator	Outcomes
1	What are the indications for SRS alone for patients with intact brain metastases?			
	Patients with intact brain metastases	Observation WBRT	SRS	Intracranial control Progression-free survival Overall survival Neurocognitive function Patient-reported outcomes
2	What are the indications for observation, preoperative SRS, or postoperative SRS or WBRT in patients with resected brain metastases?			
	Patients with resected brain metastases	Observation WBRT	SRS	Intracranial control Progression-free survival Overall survival Neurocognitive function Patient-reported outcomes
3	What are the indications for WBRT for patients with intact brain metastases?			
	Patients with intact brain metastases	Observation SRS	Conventional WBRT HA-WBRT HA-WBRT plus memantine	Intracranial control Progression-free survival Overall survival Neurocognitive function Patient-reported outcomes
4	What are the risks of symptomatic radionecrosis with WBRT and/or SRS for patients with brain metastases?			
	Patients with brain metastases	WBRT	SRS	Symptomatic radionecrosis Other adverse effects

NOTE. Table 1 is modified from "Radiation Therapy for Brain Metastases: An ASTRO Clinical Practice Guideline."²

Abbreviations: HA-WBRT, hippocampal-avoidance whole-brain radiation therapy; KQ, key question; PICO, Population, Intervention, Comparator, Outcome; SRS, stereotactic radiosurgery; WBRT, whole-brain radiation therapy.

endorsement was approved by ASCO's Evidence Based Medicine Committee on February 4, 2022.

DISCUSSION

ASCO commends ASTRO on the development of this important guideline. During the Panel's deliberations, only one recommendation, KQ2.3, was considered to warrant extra commentary. In the joint guideline,¹ the panel was unable to make a recommendation for or against any particular sequence of radiation therapy and surgery. The ASTRO guideline conditionally recommends preoperative stereotactic radiosurgery (SRS) as an alternative to postoperative SRS; however, the recommendation is weak, and it is clear in both in the table and text of the guideline that the evidence underpinning this recommendation is of low quality. The ASCO endorsement panel agrees that the strength of the recommendation and assessment of quality of the evidence accurately reflect the state of the science as written and are appropriate to its target audience. Additionally, although the ASTRO guideline does not directly address the interval between surgery and SRS, the panel notes that in the trial by Mahajan et al,⁶ SRS was performed within 30 days of surgery. The panel encourages clinicians to ensure postoperative SRS, when considered, is performed in a timely fashion without undue delay.

Otherwise, the ASCO endorsement panel accepted the recommendations of the ASTRO guideline with little need for extra discussion as they were clearly written, they clearly

indicated the supporting evidence and strength of the recommendation, and they harmonized with the joint ASCO-SNO-ASTRO guideline recommendations.

ENDORSEMENT RECOMMENDATION

ASCO endorses "Radiation Therapy for Brain Metastases: An ASTRO Clinical Practice Guideline."²

ADDITIONAL RESOURCES

More information, including a supplement, slide sets, and clinical tools and resources, is available at www.asco.org/neurooncology-guidelines. Patient information is available at www.cancer.net. The full ASTRO guideline is available at <https://www.astro.org/Patient-Care-and-Research/Clinical-Practice-Statements>.

RELATED ASCO GUIDELINES

- Integration of Palliative Care into Standard Oncology Care⁷ (<http://ascopubs.org/doi/10.1200/JCO.2016.70.1474>)
- Patient-Clinician Communication⁸ (<http://ascopubs.org/doi/10.1200/JCO.2017.75.2311>)
- Treatment of Brain Metastases: ASCO-SNO-ASTRO Guideline¹ (<https://ascopubs.org/doi/10.1200/JCO.21.02314>)

AFFILIATIONS

- ¹University of Virginia Medical Center, Charlottesville, VA
²American Society of Clinical Oncology, Alexandria, VA
³Massachusetts General Hospital, Boston, MA
⁴Mayo Clinic Cancer Center, Rochester, MN
⁵Levine Cancer Institute at Atrium Health, Charlotte, NC
⁶Stephenson Cancer Center at the University of Oklahoma, Oklahoma City, OK
⁷Banner MD Anderson Cancer Center, Loveland, CO
⁸University of Colorado School of Medicine, Aurora, CO
⁹Northwestern Medicine Cancer Center Warrenville and Proton Center, Warrenville, IL
¹⁰GRASP (Guiding Researchers & Advocates to Scientific Partnerships), Baltimore, MD
¹¹University of Rochester Medical Center, Rochester, NY
¹²Capital Health Medical Center, Pennington, NJ
¹³Cleveland Clinic, Cleveland, OH
¹⁴NYU Grossman School of Medicine, New York, NY
¹⁵Brain Tumor Center at Erasmus MC Cancer Institute, Rotterdam, the Netherlands
¹⁶University of Vermont, Burlington, VT
¹⁷University of Toronto, Toronto, ON, Canada
¹⁸Moffit Cancer Center, Tampa, FL

CORRESPONDING AUTHOR

American Society of Clinical Oncology, 2318 Mill Rd, Suite 800, Alexandria, VA 22314; e-mail: guidelines@asco.org.

EDITOR'S NOTE

This American Society of Clinical Oncology (ASCO) Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional

information, including a supplement with additional evidence tables, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/neurooncology-guidelines.

EQUAL CONTRIBUTION

D.S. and M.A.V. were Endorsement Panel cochairs.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI <https://doi.org/10.1200/JCO.22.00333>.

AUTHOR CONTRIBUTIONS

Conception and design: David Schiff, Hans Messersmith, Priscilla K. Brastianos, Ian F. Dunn, Vinai Gondi, Julia Maues, Gelareh Zadeh
Collection and assembly of data: David Schiff, Hans Messersmith, Stuart Burri, Julia Maues, Martin van den Bent
Data analysis and interpretation: David Schiff, Hans Messersmith, Priscilla K. Brastianos, Paul D. Brown, Stuart Burri, Ian F. Dunn, Laurie E. Gaspar, Justin T. Jordan, Julia Maues, Nimish Mohile, Navid Redjal, Glen H.J. Stevens, Erik P. Sulman, Martin van den Bent, H. James Wallace
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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REFERENCES

- Vogelbaum MA, Brown PD, Messersmith H, et al: Treatment for brain metastases: ASCO-SNO-ASTRO guideline. *J Clin Oncol* 40:492-516, 2022
- Gondi V, Bauman G, Bradfield L, et al: Radiation therapy for brain metastases: An ASTRO clinical practice guideline. *Pract Radiat Oncol* 10.1016/j.prro.2022.02.003 [epub ahead of print on May 6, 2022]
- ASTRO Patient Care and Research. Clinical Practice Guidelines Development Process. <https://www.astro.org/Patient-Care-and-Research/Clinical-Practice-Statements/ASTRO-39;s-Guideline-Development-Process>
- Garsa A, Jang JK, Baxi S, et al: Radiation therapy for brain metastases: A systematic review. *Pract Radiat Oncol* 11:354-356, 2021
- Brouwers MC, Kho ME, Browman GP, et al: AGREE II: Advancing guideline development, reporting and evaluation in health care. *CMAJ* 182:E839-E842, 2010
- Mahajan A, Ahmed S, McAleer MF, et al: Post-operative stereotactic radiosurgery versus observation for completely resected brain metastases: A single-centre, randomised, controlled, phase 3 trial. *Lancet Oncol* 18:1040-1048, 2017
- Ferrell BR, Temel JS, Temin S, et al: Integration of palliative care into standard oncology care: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 35:96-112, 2017
- Gilligan T, Coyle N, Frankel RM, et al: Patient-clinician communication: American Society of Clinical Oncology consensus guideline. *J Clin Oncol* 35:3618-3632, 2017



AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**Radiation Therapy for Brain Metastases: ASCO Guideline Endorsement of ASTRO Guideline**

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David Schiff

Consulting or Advisory Role: Orbus Therapeutics, GlaxoSmithKline, PRA, AstraZeneca

Research Funding: Bayer (Inst)

Priscilla K. Brastianos

Honoraria: Pfizer

Consulting or Advisory Role: ElevateBio, Dantari Pharmaceuticals, SK Life Sciences, Pfizer, Voyager Therapeutics, Sintetica, Advise Connect Inspire

Research Funding: Merck (Inst), Bristol Myers Squibb (Inst), Lilly (Inst), Mirati Therapeutics (Inst)

Paul D. Brown

Honoraria: UpToDate

Stuart Burri

Employment: Southeast Radiation Oncology Group

Stock and Other Ownership Interests: Southeast Radiation Oncology Group, Radiation Oncology Centers of the Carolinas

Travel, Accommodations, Expenses: Novocure

Other Relationship: Novocure

Laurie E. Gaspar

Employment: Banner MD Anderson Colorado

Speakers' Bureau: Cancer Experts Now

Other Relationship: NCI

Open Payments Link: <https://openpaymentsdata.cms.gov/physician/275039>

Vinai Gondi

Honoraria: UpToDate

Justin T. Jordan

Stock and Other Ownership Interests: Navio Theragnostics

Honoraria: CEC Oncology

Consulting or Advisory Role: Guidepoint Global, ClearView Healthcare Partners, Recursion Pharmaceuticals, GLG, CereXis, Navio Theragnostics, Health2047, EMP Advisory

Patents, Royalties, Other Intellectual Property: textbook royalties

Expert Testimony: Medical Mutual Insurance of Maine

Other Relationship: Shepherd Therapeutics, Shepherd Foundation, Neurofibromatosis Network, American Academy of Neurology (AAN)

Julia Maues

Honoraria: Pfizer, AstraZeneca

Consulting or Advisory Role: AstraZeneca

Nimish Mohile

Consulting or Advisory Role: Sapience Therapeutics

Research Funding: Vascular Biogenics, Boston Biomedical, Quell, Tocagen

Glen H.J. Stevens

Consulting or Advisory Role: EBSCO Industries, Inc

Erik P. Sulman

Honoraria: Novocure, Zai Lab

Research Funding: Novocure (Inst)

Martin van den Bent

Employment: AstraZeneca

Consulting or Advisory Role: AbbVie, Bristol Myers Squibb, Celgene, Agios, Boehringer Ingelheim, Bayer, carthera, Genenta Science, Nerviano Medical Sciences, Boston Pharmaceuticals

Research Funding: AbbVie (Inst)

Michael A. Vogelbaum

Stock and Other Ownership Interests: Infusion Therapeutics

Honoraria: Tocagen, Celgene, Cellinta, Plus Therapeutics

Research Funding: Infusion Therapeutics (Inst), Celgene (Inst), Oncosynergy (Inst), Olympus (Inst), Denovo Biopharma (Inst)

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No other potential conflicts of interest were reported.

APPENDIX

TABLE A1. Radiation Therapy for Brain Metastases Endorsement Expert Panel Membership

Name	Affiliation or Institution	Role and/or Area of Expertise
David Schiff, MD, co-chair	University of Virginia Medical Center, Charlottesville, VA	Neuro-oncology
Michael Vogelbaum, MD, PhD, cochair	Moffitt Cancer Center, Tampa, FL	Neurosurgical Oncology
Priscilla K. Brastianos, MD	Massachusetts General Hospital, Boston, MA	Neuro-oncology
Paul Brown, MD	Mayo Clinic Cancer Center, Rochester, MN	Radiation Oncology, Chair of the ASTRO guideline panel
Stuart Burri, MD	Levine Cancer Institute at Atrium Health, Charlotte, NC	Radiation Oncology, Member of the ASTRO guideline panel
Ian F. Dunn, MD	Stephenson Cancer Center at the University of Oklahoma, Oklahoma City, OK	Neurosurgical Oncology
Laurie E. Gaspar, MD, MBA	Banner MD Anderson Cancer Center, Loveland, CO & University of Colorado School of Medicine, Aurora, CO	Radiation Oncology
Vinai Gondi, MD	Northwestern Medicine Cancer Center Warrenville and Proton Center, Warrenville, IL	Radiation Oncology, Vice Chair of the ASTRO guideline panel
Justin T. Jordan, MD, MPH	Massachusetts General Hospital, Boston, MA	Neuro-oncology
Julia Maues, MA	GRASP (Guiding Researchers & Advocates to Scientific Partnerships), Baltimore, MD	Patient Representative
Nimish Mohile, MD	University of Rochester Medical Center, Rochester, NY	Neuro-oncology
Navid Redjal, MD	Capital Health Medical Center, Pennington, NJ	Neurosurgical Oncology
Glen H.J. Stevens, DO, PhD	Cleveland Clinic, Cleveland, OH	Neuro-oncology
Erik P. Sulman, MD, PhD	NYU Grossman School of Medicine, New York, NY	Radiation Oncology
Martin van den Bent, MD	Brain Tumor Center at Erasmus MC Cancer Institute, Rotterdam, the Netherlands	Neurology
H. James Wallace, MD	University of Vermont, Burlington, VT	PGIN Representative, Radiation Oncology
Gelareh Zadeh, MD, PhD	University of Toronto, Toronto, ON, Canada	Neurosurgical Oncology
Hans Messersmith, MPH	American Society of Clinical Oncology (ASCO), Alexandria, VA	ASCO Practice Guideline Staff (Health Research Methods)

TABLE A2. ASTRO Recommendation Grading Classification System

ASTRO's recommendations are based on evaluation of multiple factors including the QoE, and panel consensus, which among other considerations inform the strength of recommendation. QoE is based on the body of evidence available for a particular key question and includes consideration of number of studies, study design, adequacy of sample sizes, consistency of findings across studies, and generalizability of samples, settings, and treatments

Strength of Recommendation	Definition	Overall QoE Grade	Recommendation Wording
Strong	Benefits clearly outweigh risks and burden, or risks and burden clearly outweigh benefits All or almost all informed people would make the recommended choice	Any (usually high, moderate, or expert opinion)	Recommend/should
Conditional	Benefits are finely balanced with risks and burden or appreciable uncertainty exists about the magnitude of benefits and risks Most informed people would choose the recommended course of action, but a substantial number would not A shared decision-making approach regarding patient values and preferences is particularly important	Any (usually moderate, low, or expert opinion)	Conditionally recommend

Overall QoE Grade	Type/Quality of Study	Evidence Interpretation
High	Two or more well-conducted and highly generalizable RCTs or meta-analyses of such trials	The true effect is very likely to lie close to the estimate of the effect on the basis of the body of evidence
Moderate	One well-conducted and highly generalizable RCT or a meta-analysis of such trials OR Two or more RCTs with some weaknesses of procedure or generalizability OR Two or more strong observational studies with consistent findings	The true effect is likely to be close to the estimate of the effect on the basis of the body of evidence, but it is possible that it is substantially different
Low	One RCT with some weaknesses of procedure or generalizability OR One or more RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes OR Two or more observational studies with inconsistent findings, small sample sizes, or other problems that potentially confound interpretation of data	The true effect may be substantially different from the estimate of the effect. There is a risk that future research may significantly alter the estimate of the effect size or the interpretation of the results
Expert opinion ^a	Consensus of the panel on the basis of clinical judgment and experience, because of absence of evidence or limitations in evidence	Strong consensus ($\geq 90\%$) of the panel guides the recommendation despite insufficient evidence to discern the true magnitude and direction of the net effect. Further research may better inform the topic

NOTE. ASTRO's methodology allows for use of implementation remarks meant to convey clinically practical information that may enhance the interpretation and application of the recommendation. Although each recommendation is graded according to recommendation strength and QoE, these grades should not be assumed to extend to the implementation remarks.

Abbreviations: ASTRO, American Society for Radiation Oncology; QoE, quality of evidence; RCTs, randomized controlled trials.

^aA lower quality of evidence, including expert opinion, does not imply that the recommendation is conditional. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials, but there still may be consensus that the benefits of a treatment or diagnostic test clearly outweigh its risks and burden.