Proceedings from a Satellite Symposium during the
18th Annual Scientific Meeting of the Society for Neuro-Oncology

CNS TUMOR PANEL AND JOURNAL CLUB

Clinical Investigators Provide Perspectives on Current Cases and Key Presentations and Publications

CME INFORMATION

TARGET AUDIENCE

This activity is intended for neuro-oncologists, neurosurgeons and other neuro-oncology specialists involved in the treatment of primary and metastatic central nervous system (CNS) cancers.

OVERVIEW OF ACTIVITY

Brain tumors are a diverse group of neoplasms arising from different cells within the CNS or from systemic tumors that have metastasized to the CNS. Primary brain tumors include a number of histologic types with markedly different tumor growth rates and are divided into anaplastic gliomas (anaplastic astrocytoma, anaplastic oligodendroglioma and anaplastic oligoastrocytoma) and glioblastoma multiforme (GBM) based on their histopathologic features. Despite treatment, the median survival for anaplastic oligodendroglioma is 2 to 3 years, and patients with GBM can succumb to their disease within a year of onset. Thus, clinical education regarding standard and evolving best-practice therapeutic management of these neoplasms is essential to improving patient outcomes. To bridge the gap between research and patient care, these proceedings from a case-based CME symposium during the 18th Annual Meeting of the Society for Neuro-Oncology use the perspectives of leading neuro-oncologists and neurosurgeons to apply evidence-based concepts to routine practice. By providing information on the latest research developments in the context of expert perspectives, this activity assists medical oncologists with the formulation of state-of-the-art clinical management strategies, which in turn facilitates optimal patient care.

LEARNING OBJECTIVES

- Ensure delivery of appropriate treatment for primary brain cancer through the facilitation of a multidisciplinary care plan.
- Apply the results of existing and emerging research to the evidence-based use of chemotherapy and adjuvant chemoradiation therapy for patients with Grade IV GBM.
- Communicate the benefits and risks of bevacizumab, both with and without chemotherapy, to patients with newly diagnosed or recurrent GBM.
- Describe the scientific rationale and recent research results that support ongoing investigation of novel treatments for patients with brain cancer.
- Incorporate key recent clinical trial data into treatment planning for patients with primary CNS lymphomas.
- Recall the design and eligibility criteria for ongoing clinical trials, and consider appropriate patients for study participation.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 2.25 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should watch the video, complete the Post-test with a score of 75% or better and fill out the Educational Assessment and Credit Form located at ResearchToPractice.com/SNO13/CME.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

FACULTY — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

Tracy Batchelor, MD, MPH
Executive Director
Stephen E and Catherine Pappas Center for Neuro-Oncology
Massachusetts General Hospital Cancer Center
Giovanni Armenise-Harvard Professor of Neurology
Harvard Medical School
Neurologist
Massachusetts General Hospital
Boston, Massachusetts

Consulting Agreements: EMD Serono Inc, Merck, Novartis Pharmaceuticals Corporation, Roche Laboratories Inc; **Contracted Research:** AstraZeneca Pharmaceuticals LP, Millennium: The Takeda Oncology Company, Pfizer Inc.

Nicholas Butowski, MD
Associate Professor
Department of Neurological Surgery
Division of Neuro-Oncology
University of California, San Francisco
San Francisco, California

Contracted Research: Lilly; **Speakers Bureau:** Genentech BioOncology, Roche Laboratories Inc.

Howard Colman, MD, PhD
Director of Medical Neuro-Oncology
Associate Professor
Department of Neurosurgery
Huntsman Cancer Institute
University of Utah
Salt Lake City, Utah

Advisory Committee: Novocure, Roche Laboratories Inc; **Honoraria:** Merck; **Royalties:** Castle Biosciences Incorporated.

Minesh Mehta, MD
Professor, Radiation Oncology
University of Maryland
Baltimore, Maryland

Board of Directors: Pharmacyclics Inc; **Consulting Agreements:** Abbott Laboratories, Bristol-Myers Squibb Company, Elekta, Genentech BioOncology, Merck, Novelos Therapeutics Inc, Novocure, Phillips HealthCare Services Ltd; **Speakers Bureau:** Merck; **Stock Ownership:** Accuray.

Michael A Vogelbaum, MD, PhD
Professor of Surgery (Neurosurgery)
The Robert W and Kathryn B Lamborn Chair
for Neuro-Oncology
Cleveland Clinic Lerner College of Medicine
of Case Western Reserve University
Associate Director
Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center
Cleveland Clinic
Cleveland, Ohio

Consulting Agreement: Merck; Data Safety Monitoring Committee: Neuralstem Inc; **Ownership Interest:** Infuseon Therapeutics Inc.

MODERATOR — Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Algeta US, Allos Therapeutics, Amgen Inc, ArQule Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, Biodesix Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, EMD Serono Inc, Exelixis Inc, Foundation Medicine Inc, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Incyte Corporation, Lilly, Medivation Inc, Merck, Millennium: The Takeda Oncology Company, Mundipharma International Limited, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals Inc, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Spectrum Pharmaceuticals Inc and Teva Oncology.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no real or apparent conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

This activity is supported by educational grants from Genentech BioOncology and Novocure.

Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: February 2014

Expiration date: February 2015

SELECT PUBLICATIONS

Tracy Batchelor, MD, MPH

Correa DD et al. **Cognitive functions in primary central nervous system lymphoma: Literature review and assessment guidelines.** *Ann Oncol* 2007;18(7):1145-51.

Doolittle ND et al. **Long-term cognitive function, neuroimaging, and quality of life in primary CNS lymphoma.** *Neurology* 2013;81(1):84-92.

Juergens A et al. **Long-term survival with favorable cognitive outcome after chemotherapy in primary central nervous system lymphoma.** *Ann Neurol* 2010;67(2):182-9.

Lai R et al. **Treatment-induced leukoencephalopathy in primary CNS lymphoma: A clinical and autopsy study.** *Neurology* 2004;62(3):451-6.

Morris PG et al. **Rituximab, methotrexate, procarbazine, and vincristine followed by consolidation reduced-dose whole-brain radiotherapy and cytarabine in newly diagnosed primary CNS lymphoma: Final results and long-term outcome.** *J Clin Oncol* 2013;31(31):3971-9.

Nguyen PL et al. **Results of whole-brain radiation as salvage of methotrexate failure for immunocompetent patients with primary CNS lymphoma.** *J Clin Oncol* 2005;23(7):1507-13.

Omuro AMP et al. **Multicenter randomized phase II trial of methotrexate (MTX) and temozolomide (TMZ) versus MTX, procarbazine, vincristine, and cytarabine for primary CNS lymphoma (PCNSL) in the elderly: An Anocef and Goelams Intergroup study.** *Proc ASCO* 2013;**Abstract 2032**.

Rubenstein JL et al. **Intensive chemotherapy and immunotherapy in patients with newly diagnosed primary CNS lymphoma: CALGB 50202 (Alliance 50202).** *J Clin Oncol* 2013;31(25):3061-8.

Thiel E et al. **High-dose methotrexate with or without whole brain radiotherapy for primary CNS lymphoma (G-PCNSL-SG-1): A phase 3, randomised, non-inferiority trial.** *Lancet Oncol* 2010;11(11):1036-47.

Nicholas Butowski, MD

Armstrong TS et al. **Comparative impact of treatment on patient reported outcomes (PROs) in patients with glioblastoma (GBM) enrolled in RTOG 0825.** *Proc ASCO* 2013;**Abstract 2003**.

Chinot O et al. **Phase III trial of bevacizumab added to standard radiotherapy and temozolomide for newly-diagnosed glioblastoma: Mature progression-free survival and preliminary overall survival results in AVAglio.** SNO 2012;**Abstract OT-03**.

Gilbert MR et al. **RTOG 0825: Phase III double-blind placebo-controlled trial evaluating bevacizumab (Bev) in patients (Pts) with newly diagnosed glioblastoma (GBM).** *Proc ASCO* 2013;**Abstract 1**.

Henriksson R et al. **Progression-free survival (PFS) and health-related quality of life (HRQoL) in AVAglio, a phase III study of bevacizumab (Bv), temozolomide (T), and radiotherapy (RT) in newly diagnosed glioblastoma (GBM).** *Proc ASCO* 2013;**Abstract 2005**.

Johnson DR et al. **Glioblastoma survival in the United States improved after Food and Drug Administration approval of bevacizumab: A population-based analysis.** *Cancer* 2013;119(19):3489-95.

Saran F et al. **The addition of bevacizumab (BEV) to temozolomide (TMZ) and radiation therapy (RT) in newly diagnosed glioblastoma (GBM) improves progression-free survival (PFS) without adding to RT toxicity.** ASTRO 2013;**Abstract 37**.

Sulman EP et al. **Molecular predictors of outcome and response to bevacizumab (BEV) based on analysis of RTOG 0825, a phase III trial comparing chemoradiation (CRT) with and without BEV in patients with newly diagnosed glioblastoma (GBM).** *Proc ASCO* 2013;**Abstract LBA2010**.

Wefel JS et al. **Neurocognitive function (NCF) outcomes in patients with glioblastoma (GBM) enrolled in RTOG 0825.** *Proc ASCO* 2013;**Abstract 2004**.

Wick W et al. **Tumor response based on adapted Macdonald criteria and assessment of pseudoprogression (PsPD) in the phase III AVAglio trial of bevacizumab (Bv) plus temozolomide (T) plus radiotherapy (RT) in newly diagnosed glioblastoma (GBM).** *Proc ASCO* 2013;**Abstract 2002**.

Howard Colman, MD, PhD

Kesari S et al. **Phase III trial of tumor-treating fields (TTFields) together with temozolomide compared with temozolomide (TMZ) alone in patients with newly diagnosed glioblastoma multiforme (NCT00916409).** *Proc ASCO* 2012;**Abstract TPS2106**.

Kirson ED et al. **Alternating electric fields arrest cell proliferation in animal tumor models and human brain tumors.** *Proc Natl Acad Sci USA* 2007;104(24):10152-7.

Kirson ED et al. **Disruption of cancer cell replication by alternating electric fields.** *Cancer Res* 2004;64(9):3288-95.

Raizer JJ et al. **BTTC08-01: A phase II study of bevacizumab and erlotinib after radiation therapy and temozolomide in patients with newly diagnosed glioblastoma (GBM) without *MGMT* promoter methylation.** *Proc ASCO* 2013;**Abstract 2019**.

Reardon D et al. **ReACT: A phase II study of rindopepimut vaccine (CDX-110) plus bevacizumab in relapsed glioblastoma.** SNO 2013;Abstract IT-018.

Reardon DA et al. **REACT: A phase II study of rindopepimut (CDX-110) plus bevacizumab (BV) in relapsed glioblastoma (GB).** *Proc ASCO* 2012;**Abstract TPS2103**.

Stupp R et al. **NovoTTF-100A versus physician's choice chemotherapy in recurrent glioblastoma: A randomised phase III trial of a novel treatment modality.** *Eur J Cancer* 2012;48(14):2192-202.

Westphal M et al. **Adenovirus-mediated gene therapy with sitimagene ceradenovec followed by intravenous ganciclovir for patients with operable high-grade glioma (ASPECT): A randomised, open-label, phase 3 trial.** *Lancet Oncol* 2013;14(9):823-33.

Wong ET et al. **Analysis of the response profile to NovoTTF-100A treatment in patients with recurrent GBM: Time to effect, response duration and transient progressions in the EF-11 phase III trial.** SNO 2012;**Abstract NO-47**.

Minesh Mehta, MD

Furuse M et al. **Bevacizumab treatment for symptomatic radiation necrosis diagnosed by amino acid PET.** *Jpn J Clin Oncol* 2013;43(3):337-41.

Furuse M et al. **Bevacizumab for progressive radiation necrosis: Preliminary results and ongoing clinical trial.** SNO 2012;**Abstract OT-01**.

Perry JR et al. **A phase III randomized controlled trial of short-course radiotherapy with or without concomitant and adjuvant temozolomide in elderly patients with glioblastoma (NCIC CTG CE.6, EORTC 26062-22061, TROG 08.02, NCT00482677).** *Proc ASCO* 2012;**Abstract TPS2104**.

Stupp R et al. **Cilengitide combined with standard treatment for patients with newly diagnosed glioblastoma and methylated O6-methylguanine-DNA methyltransferase (MGMT) gene promoter: Key results of the multicenter, randomized, open-label, controlled, phase III CENTRIC study.** *Proc ASCO* 2013;**Abstract LBA2009**.

Tabatabai G, Weller M. **Bevacizumab plus radiotherapy for elderly patients with glioblastoma (ARTE).** *Proc ASCO* 2012;Abstract TPS2105.

Zhou LF et al. **The Stupp regimen preceded by early post-surgery temozolomide versus the Stupp regimen alone in the treatment of patients with newly diagnosed glioblastoma multiforme (GBM).** *Proc ASCO* 2013;**Abstract 2022**.

Michael A Vogelbaum, MD, PhD

Baumert BG et al. **Temozolomide chemotherapy versus radiotherapy in molecularly characterized (1p loss) low-grade glioma: A randomized phase III intergroup study by the EORTC/NCIC-CTG/TROG/MRC-CTU (EORTC 22033-26033).** *Proc ASCO* 2013;**Abstract 2007**.

Fisher BJ et al. **A phase II study of a temozolomide-based chemoradiotherapy regimen for high-risk low-grade gliomas: Preliminary results of RTOG 0424.** *Proc ASCO* 2013;**Abstract 2008**.

Lacroix M et al. **A multivariate analysis of 416 patients with glioblastoma multiforme: Prognosis, extent of resection, and survival.** *J Neurosurg* 2001;95(2):190-8.

McGirt MJ et al. **Association of surgically acquired motor and language deficits on overall survival after resection of glioblastoma multiforme.** *Neurosurgery* 2009;65(3):463-9.

Stummer W et al. **Counterbalancing risks and gains from extended resections in malignant glioma surgery: A supplemental analysis from the randomized 5-aminolevulinic acid glioma resection study. Clinical article.** *J Neurosurg* 2011;114(3):613-23.