Glioblastoma Tumor Panel and Journal Club

Clinical Investigators Provide Perspectives on Current Cases from Their Practices and Important Recent Publications and Presentations

CME Information

TARGET AUDIENCE

This activity is intended for neuro-oncologists, neurosurgeons, basic scientists and other neuro-oncology specialists involved in the treatment of primary and metastatic central nervous system cancer.

OVERVIEW OF ACTIVITY

Current management of high-grade malignant gliomas involves an interdisciplinary approach, integrating the knowledge and expertise of neurosurgeons, radiation oncologists, neuroradiologists, neuro-oncologists and medical oncologists. The historical mainstay of initial therapy for glioblastoma multiforme (GBM) has included surgical resection, when feasible, and postoperative radiation therapy. Despite the substantial contribution of effective chemoradiation therapy to the current glioma treatment algorithm, treatment of these tumors remains a clinical challenge to physicians. Median progression-free and overall survival times achieved continue to be suboptimal, at 6.9 and 14.6 months, respectively, and recurrent disease is virtually inevitable and carries a poor prognosis.

However, recent advances in the understanding of glioma pathophysiology and mechanisms of resistance to standard chemotherapeutics in addition to improvements in medication delivery across the blood-brain barrier have offered opportunities to enhance available treatment options. Furthermore, a number of efforts are ongoing in an attempt to find new therapies that may eventually confer increased quantity and quality of life for patients with brain cancer. Integrating these findings into routine clinical care, extrapolating data among histologic subtypes and communicating the benefits and risks of novel regimens to patients represent a challenge for treating clinicians. To bridge the gap between research and patient care, these proceedings from a CME symposium during the 20th 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 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 patients with primary brain cancer through facilitation of a multidisciplinary care plan.
- Use clinical and molecular markers to assess disease prognosis and guide treatment selection, when appropriate, for patients with GBM.
- Apply the results of existing and emerging research to the evidence-based use of chemotherapy and adjuvant chemoradiation therapy.
- Communicate the benefits and risks of bevacizumab, both with and without chemotherapy, to patients with recurrent GBM.
- Discuss with patients the incidence and presentation of common bevacizumab-associated adverse effects, and recommend management strategies to address tolerability issues.
- Recall available efficacy and safety data with the use of the NovoTTF-100A system for patients with newly diagnosed and recurrent GBM in order to make an informed decision regarding its incorporation into clinical practice.
- Recognize techniques to distinguish true disease progression from radiologic pseudoprogression among patients with treated brain tumors.
- Describe the scientific rationale and recent research results that support ongoing investigation of novel treatments for brain cancer.

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

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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

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Select Publications

Minesh Mehta, MD

Chakravarti A et al. **Temozolomide-mediated radiation enhancement in glioblastoma: A report on underlying mechanisms.** *Clin Cancer Res* 2006;12(15):4738-46.

Hegi M et al. **Withholding temozolomide in glioblastoma patients with unmethylated MGMT promoter — Still a dilemma?** *Neuro Oncol* 2015;17(11):1425-7.

Hegi M et al. **MGMT gene silencing and benefit from temozolomide in glioblastoma.** *N Engl J Med* 2005;352(10):997-1003.

Sandmann T et al. **Patients with proneural glioblastoma may derive overall survival benefit from the addition of bevacizumab to first-line radiotherapy and temozolomide: Retrospective analysis of the AVAglio trial.** *J Clin Oncol* 2015;33(25):2735-44.

Stupp R et al. **Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial.** *Lancet Oncol* 2009;10(5):459-66.

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**.

Tom Mikkelsen, MD

Cloughesy TF et al. **Onartuzumab plus bevacizumab versus placebo plus bevacizumab in recurrent glioblastoma (GBM): HGF and MGMT biomarker data.** *Proc ASCO* 2015;**Abstract 2015**.

Hovey EJ et al. **Continuing or ceasing bevacizumab at disease progression: Results from the CABARET study, a prospective randomized phase II trial in patients with recurrent glioblastoma.** *Proc ASCO* 2015;**Abstract 2003**.

Piccioni DE et al. **Deferred use of bevacizumab for recurrent glioblastoma is not associated with diminished efficacy.** *Neuro Oncol* 2014;16(6):815-22.

Taal W et al. **Single-agent bevacizumab or lomustine versus a combination of bevacizumab plus lomustine in patients with recurrent glioblastoma (BELOB trial): A randomised controlled phase 2 trial.** *Lancet Oncol* 2014;15(9):943-53.

Weathers SPS et al. **A randomized phase II trial of standard dose bevacizumab versus low dose bevacizumab plus lomustine (CCNU) in adults with recurrent glioblastoma.** *Proc ASCO* 2015;**Abstract 2005**.

Jeffrey Raizer, MD

Aguilar LK et al. **Phase II multicenter study of gene mediated cytotoxic immunotherapy as adjuvant to surgical resection for newly diagnosed malignant glioma.** *Proc ASCO* 2015;**Abstract 2010**.

Bloch O et al. **Newly diagnosed glioblastoma patients treated with an autologous heat shock protein peptide vaccine: PD-L1 expression and response to therapy.** *Proc ASCO* 2015;**Abstract 2011**.

Desjardins A et al. **Oncolytic polio/rhinovirus recombinant (PVSRIPO) against recurrent glioblastoma (GBM): Optimal dose determination.** *Proc ASCO* 2015;**Abstract 2068**.

Sampson JH et al. **Preliminary safety and activity of nivolumab and its combination with ipilimumab in recurrent glioblastoma (GBM): CHECKMATE-143.** *Proc ASCO* 2015;**Abstract 3010**.

Wen P et al. **A randomized double blind placebo-controlled phase 2 trial of dendritic cell (DC) vaccine ICT-107 following standard treatment in newly diagnosed patients with GBM.** *Proc SNO* 2014;**Abstract AT-60**.

Zvi Ram, MD

Pencovich N et al. **Tumor treating fields-mediated gene expression in patients with GBM.** *Proc SNO* 2015;**Abstract ATCT-26**.

Stupp R et al. **Tumor treating fields (TTFields): A novel treatment modality added to standard chemo- and radiotherapy in newly diagnosed glioblastoma — First report of the full dataset of the EF14 randomized phase III trial.** *Proc ASCO* 2015;**Abstract 2000**.

Patrick Y Wen, MD

A Phase 1 study evaluating the safety and pharmacokinetics of ABT-414 for subjects with glioblastoma multiforme. **NCT01800695**

A randomized, placebo controlled Phase 2b/3 study of ABT-414 with concurrent chemoradiation and adjuvant temozolomide in subjects with newly diagnosed glioblastoma (GBM) with epidermal growth factor receptor (EGFR) amplification (Intellance 1). **NCT02573324**

Select Publications

Al-Nedawi K et al. **Intercellular transfer of the oncogenic receptor EGFRvIII by microvesicles derived from tumour cells.** *Nat Cell Biol* 2008;10(5):619-24.

An international, randomized, double-blind, controlled study of rindopepimut/GM-CSF with adjuvant temozolomide in patients with newly diagnosed, surgically resected, EGFRvIII-positive glioblastoma. NCT01480479

Brennan CW et al. **The somatic genomic landscape of glioblastoma.** *Cell* 2013;155(2):462-77.

Fan QW et al. **EGFR phosphorylates tumor-derived EGFRvIII driving STAT3/5 and progression in glioblastoma.** *Cancer Cell* 2013;24(4):438-49.

Friedman HS et al. **Bevacizumab alone and in combination with irinotecan in recurrent glioblastoma.** *J Clin Oncol* 2009;27(28):4733-40.

Gan HK et al. **Phase I study of ABT-414 mono- or combination therapy with temozolomide (TMZ) in recurrent glioblastoma (GBM).** *Proc ASCO* 2015;**Abstract 2016**.

Inda MM et al. **Tumor heterogeneity is an active process maintained by a mutant EGFR-induced cytokine circuit in glioblastoma.** *Genes Dev* 2010;24(16):1731-45.

Johnson BF et al. **Vascular endothelial growth factor and immunosuppression in cancer: Current knowledge and potential for new therapy.** *Expert Opin Biol Ther* 2007;7(4):449-60.

Osada T et al. **The effect of anti-VEGF therapy on immature myeloid cell and dendritic cells in cancer patients.** *Cancer Immunol Immunother* 2008;57(8):1115-24.

Reardon DA et al. **ReACT: Overall survival from a randomized phase II study of rindopepimut (CDX-110) plus bevacizumab in relapsed glioblastoma.** *Proc ASCO* 2015;**Abstract 2009**.

Sampson JH et al. **Greater chemotherapy-induced lymphopenia enhances tumor-specific immune responses that eliminate EGFRvIII-expressing tumor cells in patients with glioblastoma.** *Neuro Oncol* 2011;13(3):324-33.

Sampson JH et al. **Immunologic escape after prolonged progression-free survival with epidermal growth factor receptor variant III peptide vaccination in patients with newly diagnosed glioblastoma.** *J Clin Oncol* 2010;28(31):4722-9.

Schuster J et al. **A phase II, multicenter trial of rindopepimut (CDX-110) in newly diagnosed glioblastoma: The ACT III study.** *Neuro Oncol* 2015;17(6):854-61.

Shrimali RK et al. **Antiangiogenic agents can increase lymphocyte infiltration into tumor and enhance the effectiveness of adoptive immunotherapy of cancer.** *Cancer Res* 2010;70(15):6171-80.

Wong A et al. **Expression of EGFRvIII in brain tumor stem cells.** *J Clin Oncol* 2008;26(15):S2002.