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Malignant Glioma™ UPDATE

Conversations with Oncology Investigators

Bridging the Gap between Research and Patient Care

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LAUNCH ISSUE

CME Certified

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Malignant Glioma Update
A Continuing Medical Education Audio Series

STATEMENT OF NEED/TARGET AUDIENCE

The incidence of malignant brain tumors has been increasing during the past 25 years, especially among the elderly, in whom growth has reached 1.2 percent per year. Astrocytic tumors account for more than 50 percent of primary brain cancers (comprising approximately 10,000 of the estimated 18,820 new CNS neoplasms in the US in 2006) and include the most frequently diagnosed gliomas in North America: the WHO Grade III anaplastic astrocytoma (AA) and the WHO Grade IV glioblastoma multiforme (GBM). Brain tumor grade is a robust prognostic factor. Despite current treatment, the overall survival rates for patients with WHO Grade III AA is two to three years, and those with Grade IV GBM generally succumb to their disease within a year from diagnosis. Thus, clinician education regarding standard and evolving optimal therapeutic management of these prevalent neoplasms is of the utmost importance to improve patient outcomes. Current management of high-grade malignant gliomas involves an interdisciplinary approach, integrating the knowledge and expertise of neurosurgeons, radiation oncologists, neuroradiologists and medical oncologists. Whereas the historical mainstay of initial therapy for both AA and GBM has included surgical resection, when feasible, and postoperative radiation therapy, recent advances in clinician understanding of glioma pathophysiology, mechanisms of resistance to standard chemotherapeutics and improvements in medication delivery across the blood-brain barrier have offered an opportunity to enhance available treatment options.

LEARNING OBJECTIVES

- Critically evaluate the implications of emerging clinical trial data focused on local and systemic treatment of primary brain tumors, and incorporate these data into management strategies in the front-line, recurrent and refractory-disease settings.
- Counsel appropriately selected patients with high-grade glioma about the availability of ongoing clinical trials.
- Describe the epidemiologic, demographic and prognostic trends for malignant gliomas, and effectively communicate this information to patients and caregivers.
- Describe the pathogenesis of high-grade gliomas, including the unique biologic and anatomic challenges relevant to the successful access, selection, activity and resistance of systemic therapeutics.
- Discuss the historic and evolving role of adjuvant chemoradiation therapy, and demonstrate the evidence-based application of this information in the management of Grade III and Grade IV gliomas.
- Develop an evidence-based treatment algorithm for the sequential use of local and systemic interventions in the management of recurrent or refractory high-grade gliomas, incorporating individualized patient risk-benefit assessments.
- Provide a summary of the scientific rationale and recent clinical trial results that support the future investigation of angiogenesis and multikinase inhibitors in the medical management of GBM.
- Communicate to patients the incidence and presentation of common treatment-associated adverse effects, and recommend management strategies to address tolerability issues.

PURPOSE OF THIS ISSUE OF *MALIGNANT GLIOMA UPDATE*

The purpose of Issue 1 of *Malignant Glioma Update* is to support the learning objectives by offering the perspectives of Drs Vredenburgh, Friedman, Raizer and Abrey on the integration of emerging clinical research data into the management of malignant gliomas.

ACCREDITATION STATEMENT

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CREDIT DESIGNATION STATEMENT

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CME INFORMATION

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Research To Practice 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 Research To Practice scientific staff and an external, independent 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: **Dr Vredenburgh** — Consulting Agreement: Genentech BioOncology. **Dr Friedman** — Advisory Committee: Bradmer Pharmaceuticals Inc, Keryx Biopharmaceuticals Inc, MGI Pharma Inc; Paid Research: MGI Pharma Inc, Schering-Plough Corporation; Speakers Bureau: MGI Pharma Inc. **Dr Raizer** — Advisory Committee and Speakers Bureau: Genentech BioOncology, Schering-Plough Corporation; Paid Research: Cephalon Inc, Eli Lilly and Company, Genentech BioOncology, Novartis Pharmaceuticals Corporation, Schering-Plough Corporation. **Dr Abrey** — Advisory Committee: Enzon Pharmaceuticals, Genentech BioOncology, Merck and Company Inc, Pfizer Inc; Consulting Agreement: Genentech BioOncology; Speakers Bureau: Schering-Plough Corporation.

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QUESTIONS (PLEASE CIRCLE ANSWER):

1. **Activation of which of the following cellular growth factor pathways stimulates malignant gliomas?**
   a. Platelet-derived growth factor (PDGF)
   b. Epidermal growth factor
   c. Vascular endothelial growth factor (VEGF)
   d. All of the above

2. **The six-month progression-free survival rate for patients with recurrent glioblastoma multiforme (GBM) who were treated with bevacizumab and _____ was 45 percent.**
   a. Temozolomide
   b. Erlotinib
   c. Irinotecan
   d. Both a and c

3. **Cediranib is a tyrosine kinase inhibitor of _____.**
   a. EGFR
   b. VEGF
   c. PDGF
   d. All of the above

4. **Which of the following side effects may occur in patients with GBM who are treated with bevacizumab?**
   a. Hypertension
   b. Fatigue
   c. Proteinuria
   d. Both a and c
   e. All of the above

5. **Which of the following agents is considered radioimmunotherapy?**
   a. Bevacizumab
   b. Temozolomide
   c. Neuradiab
   d. All of the above
   e. None of the above

6. **Neuradiab is administered _____.**
   a. Topically
   b. Intravenously
   c. Through a Rickham reservoir
   d. Subcutaneously
   e. All of the above

7. **Which of the following is a potential side effect in patients receiving the carmustine wafer for the treatment of GBM?**
   a. Bone marrow suppression
   b. Increased risk of infection
   c. Hair loss
   d. Neuropathy

8. **Coexpression of EGFRvIII and PTEN by glioblastoma cells is associated with responsiveness to erlotinib or gefitinib.**
   a. True
   b. False

9. **Temozolomide is FDA approved for the treatment of _____.**
   a. Recurrent anaplastic astrocytomas
   b. Recurrent GBM
   c. Newly diagnosed GBM in combination with radiation therapy and as maintenance therapy
   d. Both a and c
   e. All of the above

10. **The addition of temozolomide to adjuvant radiation therapy for patients with glioblastomas improves overall survival by approximately _____.**
    a. 12 months
    b. Six months
    c. 2.5 months
    d. None of the above

11. **In the Phase III clinical trial of adjuvant radiation therapy with temozolomide for patients with glioblastomas, the duration of therapy with maintenance temozolomide was _____.**
    a. Six months
    b. 12 months
    c. 24 months
    d. 36 months

12. **Clinical trials are evaluating the role of rituximab in the treatment of primary CNS lymphoma.**
    a. True
    b. False

Post-test answer key: 1d, 2c, 3b, 4e, 5c, 6c, 7b, 8a, 9d, 10c, 11a, 12a

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Malignant Glioma Update — Issue 1, 2008

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART ONE — Please tell us about your experience with this educational activity

BEFORE completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

- **Key molecular pathways in GBM** 4 3 2 1
- **Clinical experience with bevacizumab in GBM** 4 3 2 1
- **Radiation therapy and temozolomide** 4 3 2 1
- **Development of the oral anti-VEGF agent cediranib in GBM** 4 3 2 1

AFTER completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

- **Key molecular pathways in GBM** 4 3 2 1
- **Clinical experience with bevacizumab in GBM** 4 3 2 1
- **Radiation therapy and temozolomide** 4 3 2 1
- **Development of the oral anti-VEGF agent cediranib in GBM** 4 3 2 1

Was the activity evidence based, fair, balanced and free from commercial bias?

☐ Yes ☐ No

Please explain: . . . . . .

Will this activity help you improve patient care?

☐ Yes ☐ No ☐ Not applicable

If no, please explain: . . . . . .

Did the activity meet your educational needs and expectations?

☐ Yes ☐ No

If no, please explain: . . . . . .

Please respond to the following LEARNER statements by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = Learning objective not met N/A = Not applicable

As a result of this activity, I will:

- Critically evaluate the implications of emerging clinical trial data focused on local and systemic treatment of primary brain tumors, and incorporate these data into management strategies in the front-line, recurrent and refractory-disease settings. . . . . 4 3 2 1 N/M N/A
- Counsel appropriately selected patients with high-grade glioma about the availability of ongoing clinical trials. . . . . 4 3 2 1 N/M N/A
- Describe the epidemiologic, demographic and prognostic trends for malignant gliomas, and effectively communicate this information to patients and caregivers. . . . . 4 3 2 1 N/M N/A
- Describe the pathogenesis of high-grade gliomas, including the unique biologic and anatomic challenges relevant to the successful access, selection, activity and resistance of systemic therapeutics. . . . . 4 3 2 1 N/M N/A
- Discuss the historic and evolving role of adjuvant chemoradiation therapy, and demonstrate the evidence-based application of this information in the management of Grade III and Grade IV gliomas. . . . . 4 3 2 1 N/M N/A
- Develop an evidence-based treatment algorithm for the sequential use of local and systemic interventions in the management of recurrent or refractory high-grade gliomas, incorporating individualized patient risk-benefit assessments. . . . . 4 3 2 1 N/M N/A
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- Communicate to patients the incidence and presentation of common treatment-associated adverse effects, and recommend management strategies to address tolerability issues. . . . . 4 3 2 1 N/M N/A

What other practice changes will you make or consider making as a result of this activity?

. . . . . .

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

What additional information or training do you need on the activity topics or other oncology-related topics?

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Additional comments about this activity:

.....

.....

May we include you in future assessments to evaluate the effectiveness of this activity?

☐ Yes ☐ No

PART TWO — Please tell us about the faculty for this educational activity

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

Faculty	Knowledge of subject matter	Effectiveness as an educator
James J Vredenburgh, MD	4 3 2 1	4 3 2 1
Henry S Friedman, MD	4 3 2 1	4 3 2 1
Jeffrey Raizer, MD	4 3 2 1	4 3 2 1
Lauren E Abrey, MD	4 3 2 1	4 3 2 1

Please recommend additional faculty for future activities:

.....

Other comments about the faculty for this activity:

.....

REQUEST FOR CREDIT — Please print clearly

Name:..... Specialty:.....

Degree:

☐ MD ☐ DO ☐ PharmD ☐ NP ☐ BS ☐ RN ☐ PA ☐ Other .....

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I certify my actual time spent to complete this educational activity to be _____ hour(s).

Signature:..... Date:.....

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