

Conversations with Oncology Investigators Bridging the Gap between Research and Patient Care

#### FACULTY INTERVIEWS

Marc Chamberlain, MD Timothy F Cloughesy, MD

**EDITOR** 

Neil Love, MD





## CNS Cancer Update

## A Continuing Medical Education Audio Series

#### OVERVIEW OF ACTIVITY

Brain tumors are a diverse group of neoplasms arising from different cells within the central nervous system (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 the 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, this issue of CNS Cancer Update features one-on-one discussions with leading neurooncologists and neurosurgeons. 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

- Utilize case-based learning to facilitate the development of evidence-based and individualized management strategies for newly diagnosed and recurrent primary CNS cancer.
- Identify strategies to distinguish between true disease progression and radiographic pseudoprogression in patients with malignant glioma who have undergone chemoradiation therapy.
- Evaluate the prognostic and/or predictive role of molecular profiling (eg, MGMT methylation status) in primary CNS cancers.
- Develop evidence-based clinical management strategies for recurrent or progressive GBM, including the use of anti-angiogenic therapy.
- Incorporate key recent clinical trial data into treatment planning for patients with primary CNS lymphomas.
- Anticipate future protocol and nonprotocol treatment options for patients based on investigational strategies using novel targets, agents and biomarkers in CNS cancers.

#### 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 1.5 AMA PRA Category 1 Credits<sup>TM</sup>. 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 contains an audio component. To receive credit, the participant should review the CME information, listen to the CD, complete the Post-test with a score of 70% or better and fill out the Educational Assessment and Credit Form located in the back of this booklet or on our website at **ResearchToPractice.com/CNSU211/CME**.

This activity is supported by an educational grant from Genentech BioOncology.

Last review date: December 2011; Release date: December 2011; Expiration date: December 2012

If you would like to discontinue your complimentary subscription to *CNS Cancer Update*, please email us at **Info@ResearchToPractice.com**, call us at (800) 648-8654 or fax us at (305) 377-9998. Please include your full name and address, and we will remove you from the mailing list.

#### CME INFORMATION



#### **FACULTY AFFILIATIONS**



Marc Chamberlain, MD
University of Washington
Department of Neurology and
Neurological Surgery
Chief, Division of NeuroOncology, Fred Hutchinson
Cancer Research Center
Seattle Cancer Care Alliance
Seattle. Washington



Timothy F Cloughesy, MD
Professor; Director, NeuroOncology Program
Director, Henry Singleton Brain
Cancer Research Program
Department of Neurology
David Geffen School of
Medicine at UCLA
Los Angeles. California

#### **EDITOR**



Neil Love, MD Research To Practice Miami, Florida

#### 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: **Dr Chamberlain** — Advisory Committee: Genentech BioOncology, Lilly USA LLC, Mundipharma International Limited, Sigma-Tau Pharmaceuticals Inc; Paid Research: Exelixis Inc, MedImmune Inc, Myrexis Inc; Speakers Bureau: Genentech BioOncology, Schering-Plough Corporation, Sigma-Tau Pharmaceuticals Inc. **Dr Cloughesy** — Advisory Committee: Amgen Inc, Genentech BioOncology, Lilly USA LLC, Novartis Pharmaceuticals Corporation; Consulting Agreement: Roche Laboratories Inc; Speakers Bureau: Schering-Plough Corporation.

**EDITOR** — 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: Abbott Laboratories, Allos Therapeutics, Amgen Inc, Astellas Pharma Global Development Inc, Bayer HealthCare Pharmaceuticals/Onyx Pharmaceuticals Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Cephalon Inc, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, EMD Serono Inc, Genentech BioOncology, Genomic Health Inc, ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, Lilly USA LLC, Medivation Inc, Millennium: The Takeda Oncology Company, Mundipharma International Limited, Novartis Pharmaceuticals Corporation. Sanofi, Seattle Genetics and Teva Pharmaceuticals.

**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 grantor.

### CNS Cancer Update — Issue 2, 2011

#### QUESTIONS (PLEASE CIRCLE ANSWER):

- 1. The BRAIN noncomparative study demonstrated a similar overall survival for bevacizumab monotherapy and bevacizumab/irinotecan in patients with recurrent glioblastoma.
  - a. True
  - b. False
- 2. Symptomatic intratumoral hemorrhage is commonly observed in patients with recurrent GBM treated with bevacizumab.
  - a. True
  - b. False
- 3. Epileptic seizures occur in approximately 20% to 30% of patients with GBM.
  - a. True
  - b. False
- 4. MGMT methylation status in GBM appears to be
  - a. Prognostic
  - b. Predictive
  - c. Both a and b
- 5. Which of the following is generally true regarding pseudoprogression in GBM?
  - a. Mimics early disease progression
  - b. Occurs in 20% to 30% of patients with apparent radiographic progression after chemoradiation therapy
  - c. May be differentiated from true progression via magnetic resonance perfusion imaging
  - d. All of the above
- 6. Which of the following is/are correlated with IDH1 mutations in gliomas?
  - a. Lower grade
  - b. Oligodendroglial-like features
  - c. More favorable natural history
  - d. All of the above

- 7. The AVAglio and RTOG-0825 Phase III studies are evaluating the addition of \_\_\_\_\_ to standard radiation therapy with temozolomide (TMZ) for patients with newly diagnosed GBM.
  - a. Irinotecan
  - b. Cediranib
  - c. Bevacizumab
- 8. Which of the following was observed in the Phase III RTOG-0525 study of standard adjuvant TMZ versus dosedense TMZ in patients with newly diagnosed GBM?
  - Dose-dense TMZ resulted in an improvement in median overall and progression-free survival compared to standard TMZ
  - b. Dose-dense and standard TMZ were equivalent with regard to median overall and progression-free survival
  - c. MGMT methylation status was not prognostic
- Prospective, randomized studies have demonstrated improvements in overall survival with erlotinib or gefitinib among patients with GBM and EGFRVIII mutations.
  - a. True
  - b. False
- 10. In a randomized, Phase III study the NovoTTF-100A medical device resulted in no difference in time to disease progression or overall survival compared to standard chemotherapy in patients with recurrent GBM.
  - a. True
  - b. False

#### **EDUCATIONAL ASSESSMENT AND CREDIT FORM**

## CNS Cancer Update — Issue 2, 2011

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.

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

#### PART 1 — Please tell us about your experience with this educational activity

How would you characterize your level of knowledge on the following topics?

	BEFORE	AFTER
BELOB Phase II study of bevacizumab, lomustine or the combination for recurrent GBM after chemoradiation therapy with TMZ	4 3 2 1	4 3 2 1
Results of RTOG 0525: A Phase III trial of standard adjuvant TMZ versus a dose-dense schedule in newly diagnosed GBM	4 3 2 1	4 3 2 1
Phase III studies (AVAglio and RTOG-0825) incorporating bevacizumab into standard radiation therapy/TMZ in newly diagnosed GBM	4 3 2 1	4 3 2 1
Emerging data with the prognostic biomarker IDH1 in glioma	4 3 2 1	4 3 2 1
If no, please explain:  Please identify how you will change your practice as a result of complete that apply).  This activity validated my current practice; no changes will be more create/revise protocols, policies and/or procedures  Change the management and/or treatment of my patients  Other (please explain):  If you intend to implement any changes in your practice, please proving the procedure of the procedure of the please proving the proving the procedure of the please proving the procedure of the please proving the proving the proving the proving the proving the procedure of the please proving the proving	pleting this activate	vity (select all
The content of this activity matched my current (or potential) scope  Yes No If no, please explain:  Please respond to the following learning objectives (LOs) by circling		
4 = Yes $3 = Will consider$ $2 = No$ $1 = Already doing N/M = LO$	not met N/A =	Not applicable
As a result of this activity, I will be able to:  Utilize case-based learning to facilitate the development of evidence-based and individualized management strategies for newly diagnosed and recurrent primary CNS cancer.  Identify strategies to distinguish between true disease progression and radiographic pseudoprogression in patients with malignant glioma wh have undergone chemoradiation therapy.  Evaluate the prognostic and/or predictive role of molecular profiling (eg, MGMT methylation status) in primary CNS cancers.  Develop evidence-based clinical management strategies for recurren progressive GBM, including the use of anti-angiogenic therapy.  Incorporate key recent clinical trial data into treatment planning for patients with primary CNS lymphomas.  Anticipate future protocol and nonprotocol treatment options for patie based on investigational strategies using novel targets, agents and		2 1 N/M N/A 2 1 N/M N/A 2 1 N/M N/A
biomarkers in CNS cancers.	4 3	2 1 N/M N/A

#### EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

r-improve ucationa such a s ow-up st follow-up culty and od wledge of 4 3 4 3	ement el lintervey.  urvey.  survey.  d editor  2 = Add  f subje  2  of subje  2	for this ec	onduct pos profession	activition optiminess a	ctice.	Please  educator  1 1
ucationa such a s ow-up su follow-up culty and d wledge o 4 3 owledge o 4 3	I intervourvey.  arvey.  b survey.  c survey	y. for this ecequate ect matter 1 1 ect matter	lucational at 1 = Sub Effective 4 4 Effective	activitiooptimess a	ctice.	Please  educator  1 1
ucationa such a s ow-up su follow-up culty and d wledge o 4 3 owledge o 4 3	I intervourvey.  arvey.  b survey.  c survey	y. for this ecequate ect matter 1 1 ect matter	lucational at 1 = Sub Effective 4 4 Effective	activitiooptimess a	ctice.	Please  educator  1 1
culty and od whedge of 4 3 owledge of 4 3	d editor 2 = Ado of subjection 2 2 = 2 of subjection 2	for this ecequate equate 1 1 ecct matter	1 = Sub Effective 4 4 Effective	ness a	as an 2 2	1
owledge of 4 3 owledge of 4 3	2 = Ade of subject 2 = 2 of subject 2 = 2	equate  ct matter  1  1  cet matter	1 = Sub Effective 4 4 Effective	ness a	as an 2 2	1
4 3  owledge of 4 3  owledge of 4 3	of subject 2 2 pf subject 2	1 1 ect matter	Effective 4 4 Effective	ness a	2 2	1
4 3 4 3 <b>owledge</b> 4 3	2 of subjection 2	1 1 ect matter	4 4 Effective	3	2	1
4 3 <b>owledge</b> 4 3	2 of subje	1 ect matter	4 Effective	3	2	1
owledge (	of subje	ect matter	Effective			
4 3	2			ness	as an	
		1	4			educato
future ac	tivities:			3	2	1
print cl	early					
		Special	ıty			
NP (	⊃ RN	□ PA	□ Oth	er		
			Box/Su	ite:		
	Fax:					
uring ma	terial fo	or a maxim	um of 1.5	AMA .	PRA (	<i>ategory</i> ir partici
this ed	ucation	al activity t	to be		hour(s	i).
	NP (	NP RN Fax:  uring material for the credit comm	NP RN PA  Fax:  uring material for a maxim the credit commensurate	Specialty:	Specialty:  NP RN PA Other  Box/Suite:  Fax:  uring material for a maximum of 1.5 AMA the credit commensurate with the extent of	NP RN PA Other Box/Suite:

To obtain a certificate of completion and receive credit for this activity, please complete the Post-test, fill out the Educational Assessment and Credit Form and fax both to (800) 447-4310, or mail both to Research To Practice, One Biscayne Tower, 2 South Biscayne Boulevard, Suite 3600, Miami, FL 33131. You may also complete the Post-test and Educational Assessment online at www.ResearchToPractice.com/CNSU211/CME.



Editor Neil Love, MD

Managing Editor and CME Director Kathryn Ault Ziel, PhD

Scientific Director Richard Kaderman, PhD

Editorial Clayton Campbell

Gloria Kelly, PhD Jean Pak Margaret Peng

Creative Manager Fernando Rendina

> Tamara Dabney Silvana Izquierdo

Copy Editing Manager Kirsten Miller

Senior Production Editor Aura Herrmann

Copy Editors Margo Harris

David Hill

Rosemary Hulce Pat Morrissey/Havlin

Alexis Oneca

Production Manager Tracy Potter

Audio Production Frank Cesarano

Web Master John Ribeiro

Multimedia Project Manager Marie Philemon

Faculty Relations Manager Melissa Molieri

Continuing Education Administrator for Nursing Julia W Aucoin, DNS, RN-BC, CNE

Contact Information Neil Love, MD

Research To Practice One Biscayne Tower

2 South Biscayne Boulevard, Suite 3600

Miami, FL 33131 Fax: (305) 377-9998

Email: DrNeilLove@ResearchToPractice.com

For CME/CNE Information Email: CE@ResearchToPractice.com

Copyright @ 2011 Research To Practice. All rights reserved.

The compact disc, Internet content and accompanying printed material are protected by copyright. No part of this program may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording or utilizing any information storage and retrieval system, without written permission from the copyright owner.

The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantor.

Participants have an implied responsibility to use the

newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management.

Any procedures, medications or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patients' conditions and possible contraindications or dangers in use, review of any applicable manufacturer's product information and comparison with recommendations of other authorities.



Copyright © 2011 Research To Practice.
This activity is supported by an educational grant from Genentech BioOncology.

# Research To Practice®

Sponsored by Research To Practice.

Last review date: December 2011 Release date: December 2011 Expiration date: December 2012 Estimated time to complete: 1.5 hours