INTERVIEW

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Tracks 1-17

Track 1 **Case discussion:** A 60-year-old woman with an oligodendroglioma treated with surgery and adjuvant temozolomide 10 years previously followed by multiple systemic treatments undergoes external beam radiation therapy after developing focal seizures

Track 2 Classification and natural history of primary brain tumors

Track 3 Prognostic and predictive significance of 1p/19q deletion in anaplastic oligodendroglioma

Track 4 Use of bevacizumab in oligodendroglioma

Track 5 Effect of brain radiation therapy on cognitive function

Track 6 Ongoing clinical trials of temozolomide and/or radiation therapy for patients with 1p/19q codeleted oligodendroglioma

Track 7 **Case discussion:** A 28-year-old man with right-frontal GBM undergoes surgical resection followed by enrollment on a clinical trial of radiation therapy/temozolomide and erlotinib followed by multiple systemic regimens for recurrent progressive disease

Track 8 Secondary glioblastoma as a distinct subtype of GBM with a different biology

Track 9 Investigating change in intensity or pattern of chronic low-grade headaches

Track 10 **Case discussion:** A 51-year-old man with relapsed gliosarcoma develops a pulmonary embolism eight to 10 weeks after initiation of bevacizumab

Track 11 Gliosarcoma: A subset of GBM with spindle-like morphology

Track 12 Management of venous thromboembolism in patients with gliomas

Track 13 Tolerability of bevacizumab in GBM

Track 14 Pros and cons of bevacizumab versus bevacizumab/irinotecan for recurrent GBM

Track 15 Evaluation of bevacizumab as front-line therapy for GBM

Track 16 Palliative issues among patients with GBM

Track 17 Importance of immediate neurosurgical evaluation and biopsy of suspected central nervous system lymphoma

Select Excerpts from the Interview

Tracks 14-15

DR LOVE: What are your thoughts about the use of bevacizumab or irinotecan/bevacizumab for GBM?

DR PEEREBOOM: Bevacizumab is FDA approved for recurrent glioblastoma, and two clinical trials (Cloughesy 2010; [1.1, page 4]; Friedman 2009; [4.1]) have evaluated, in a randomized fashion, bevacizumab with or without irinotecan. These studies have demonstrated an improvement in progression-free survival but no improvement in overall survival when irinotecan is added to bevacizumab. Toxicity is increased with the combination, and much debate has taken place in the neurooncology community as to whether irinotecan should be used in combination with bevacizumab.

My bias is not to use the combination but rather to use bevacizumab as a single agent because I believe that in this patient population quality of life is probably at the top of the list as far as goals we are trying to accomplish. The addition of irinotecan puts a dent in patients' quality of life.

DR LOVE: What about clinical research in the up-front setting?

DR PEEREBOOM: A number of Phase II trials have evaluated bevacizumab in the up-front management of GBM. The preliminary findings from these small, single-institution studies appear encouraging. The important ongoing clinical trial is RTOG-0825 (1.3, page 6), in which patients are randomly assigned to radiation therapy/temozolomide with or without bevacizumab. This is a placebo-controlled study that will be enrolling approximately 1,000 patients.

I believe the results of this trial will answer the important question of whether up-front bevacizumab produces an improvement in survival, progression-free survival and quality of life. With well-informed patients I discuss the fact that at some point in the course of the illness bevacizumab will probably become part of their therapy. We do not know yet if using it up front is better than using it at the time of disease progression.

4.1

Randomized Phase II Trial: Bevacizumab Alone or in Combination with Irinotecan in Recurrent Glioblastoma

	Bevacizumab	Bevacizumab/ irinotecan
Overall response rate	28.2%	37.8%
Six-month progression-free survival	42.6%	50.3%
Overall survival	9.2 months	8.7 months

Friedman HS et al. *J Clin Oncol* 2009;27(28):4733-40.

Tracks 3, 6

DR LOVE: What is the significance of 1p/19q deletion in anaplastic glioma?

DR PEEREBOOM: Patients with anaplastic glioma with 1p/19q deletion have long survival rates and good sensitivity to chemotherapy and radiation therapy.

This codeletion is mediated by a translocation of 1p and 19q. At this point, the function of this translocation is not understood. The important fact, I believe, is that in this subset of high-grade gliomas, patients may not need to undergo radiation therapy at the time of diagnosis. And, although no trials have examined cognitive and quality-of-life issues, when we take one approach or the other my bias for such patients would be to delay radiation therapy.

DR LOVE: Are any clinical trials evaluating treatment for this subset?

DR PEEREBOOM: A large randomized trial is ongoing for patients with anaplastic gliomas with 1p/19q codeletion (4.2). The trial has three arms: radiation therapy alone, radiation therapy with temozolomide and temozolomide alone. This trial will teach us how to best approach this group of patients. ■

4.2

Phase III Trial Evaluating Temozolomide Alone versus Radiation Therapy Alone versus Temozolomide/Radiation Therapy in the Up-Front Management of 1p/19q Codeleted Anaplastic Glioma

Protocol IDs: NCCTG-N0577, EORTC-26081 **Target Accrual:** 488

Primary endpoint: Overall survival

Eligibility

- Histologically confirmed 1p/19q codeleted anaplastic glioma
- Mandatory central pathology review
- Surgery within three months

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- Radiation therapy alone*
- Radiation therapy + temozolomide†
- Temozolomide alone‡

* Radiation therapy is administered five days a week for six weeks. † Oral temozolomide is administered on days one through seven for six weeks. Beginning four weeks after completion of concurrent chemoradiation therapy, patients receive adjuvant oral temozolomide once daily on days one through five, q28d for six to 12 courses. ‡ Oral temozolomide is administered once daily on days one through five, q28d for 12 courses.

www.clinicaltrials.gov, October 2010.

SELECT PUBLICATIONS

Cairncross JG et al. **Specific genetic predictors of chemotherapeutic response and survival in patients with anaplastic oligodendrogliomas.** *J Natl Cancer Inst* 1998;90(19):1473-9.

Cloughesy T et al. **Updated safety and survival of patients with relapsed glioblastoma treated with bevacizumab in the BRAIN study.** *Proc ASCO* 2010;**Abstract 2008**.

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

Kim JW et al. **Relationship between radiological characteristics and combined 1p and 19q deletion in World Health Organization grade III oligodendroglial tumours.** *J Neurol Neurosurg Psychiatry* 2010;[Epub ahead of print].

Vredenburgh JJ et al. **Bevacizumab plus irinotecan in recurrent GBM.** *J Clin Oncol* 2007;25(30):4722-9.