

Neurology[®]

PCV chemotherapy for recurrent glioblastoma multiforme

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Neurology 2001;56;1782

This information is current as of September 17, 2011

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://www.neurology.org/content/56/12/1782.1.full.html>

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Table 2 Comparison of data

	PCV (Boiardi)	PCV (Kappelle)	PCV+ locoregional therapy (Boiardi)
Patient no./survival time, wk	27/29.7	63/33	20/54

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To the Editor: We read with interest the recent article by Kappelle et al.¹ They report data of a retrospective study on chemotherapy with vincristine (PCV) in 63 patients with recurrent glioblastoma.

In line with literature data,² their median time to tumor progression (TTP) and survival time (ST) values were related to young age and postsurgery Karnofsky performance status (KPS); also, they were not different in 26 patients undergoing a second resection.

We report the clinical data pertaining to 47 patients with recurrent glioblastoma followed prospectively in our institution and treated homogeneously before relapse (i.e., surgery, followed by radiotherapy and systemic chemotherapy with carmustine and cisplatin every 6 weeks).

Patients were included in the study if they were between the ages of 18 and 65 and had histological diagnosis of glioblastoma or tumor recurrence (KPS >70) as a single supratentorial lesion without subependymal diffusion with normal blood and urine tests.

In 20 of these patients (selected solely on the basis of their convenience in attending repeated outpatient visits), an Ommaya reservoir was placed in the postsurgical cavity for locoregional chemotherapy at tumor relapse.

Age and KPS were not different in patients with or without the Ommaya reservoir. At relapse, 27 patients were treated with PCV alone, whereas the 20 patients with the Ommaya reservoir also received locoregional mitoxantrone 4 mg every 20 days.

Mitoxantrone was selected on the basis of its well known tumoricidal activity on malignant glial cells and on our preliminary experience showing good tolerability and lack of significant side effects.^{3,4}

Table 2 shows the comparison between Kappelle et al.'s data and those of our patient cohort as far as ST is concerned. While our 27 patients treated with PCV alone displayed an adjunctive survival very close to that in Kappelle et al.'s series, 20 patients who also received locoregional chemotherapy showed a longer adjunctive survival.

In our series, the potential confounding biases represented by re-resection and prerelapse differences in pharmacologic management were not present.

Locoregional therapy was well tolerated and led to a prolonged adjunctive survival. We believe the cost-effectiveness should be considered in managing a malignant tumor with poor prognosis. Its impact on patients' quality of life must be better evaluated.⁵

Amerigo Boiardi, *Italy*

Reply from the Authors: We thank Dr. Boiardi for his comments on our recent article.¹ He reports results of a clinical study of 47 patients with recurrent glioblastoma multiforme treated with PCV alone (n = 27) or with PCV and locoregional mitoxantrone (n = 20). The reported (median?) survival (54 weeks) was superior in patients treated with combined therapy compared with PCV alone (29.7 weeks). The survival in the PCV-treated patients is comparable to our results. The survival of the PCV+ mitoxantrone-treated patients is comparable to survival data from other small phase I/II studies evaluating the effects of various therapies in patients with recurrent high-grade glioma, e.g., immune therapy, chemotherapy, or combined chemotherapy and stereotactic radiosurgery.⁶⁻⁸ They conclude that locoregional therapy with mitoxantrone should be considered in this setting because of prolonged survival and lack of serious side effects. However, in our opinion it is not possible to draw firm conclusions from this letter. It is not clear how patients were selected for locoregional

therapy (only on the basis of the ability to attend repeated outpatient visits, which suggests that only patients in a good condition were treated with combined therapy?), how this treatment was performed exactly (Ommaya reservoir in the initial surgical cavity?), and how reliable tumor recurrence was diagnosed and radionecrosis excluded.⁹ In addition, data on important prognostic factors such as age, Karnofsky performance status, TTP before initiation of study treatment, and data on TTP and response to study treatment are lacking. However, efficacy and safety of locoregional chemotherapy have been described earlier in patients with recurrent high-grade glioma.¹⁰ We are interested in a more detailed report of the results of locoregional mitoxantrone therapy.

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Competency to consent to medical treatment in cognitively impaired patients with Parkinson's disease

To the Editor: As a neurologist and a clinical bioethicist, I was pleased to see the article on competency¹ featured as a CME article in the January 9 issue. In general, I felt the article was well done and educational.

Unfortunately, the title of this article and much of the authors' discussion perpetuates an error. The authors are discussing decisional capacity,² medical information processing,³ capacity to consent,^{4,5} or ability to understand informed consent.⁶ Competency is a legal issue.^{7,8} The authors seem to understand this as evidenced by their final paragraph, but they attempt to establish a dichotomy between competency and legal competency. A more helpful working dichotomy, and one used in much of the bioethical literature, is between decisional capacity and legal competency.

Robert E. Cranston, MD, *Urbana, IL*

Reply from the Authors: Dr. Cranston's observation of the distinction between the terms capacity and competency presents an opportunity to clarify the meaning of these important concepts. The terms are frequently used interchangeably, even synonymously, but they are substantively different.^{9,10} We recognize that confusion about their meaning is in part a consequence of not simply what is being evaluated, but who performs the evaluation of competency (a clinician or a judge).

As Dr. Cranston suggests, we do propose a distinction between competency and legal competency. More specifically, we distinguish between three concepts: decisional capacity, competency, and legal competency. These distinctions hopefully represent a conceptual clarification and advance, rather than further confusion. *Decisional capacity* relates to a patient's general decisional abilities, such as understanding treatment information, reasoning, and appreciating consequences.¹⁰ A clinician can use a variety of assessment methods to evaluate these decisional abilities. *Competency* relates to a clinician's judgment as to whether or not a patient can carry out a specific act (e.g., consent to lumbar puncture) or set of activities (e.g., handle his/her financial affairs). A patient's decisional abilities will inform this judgment of competency. Thus, both decisional capacity and competency are clinical terms as contemplated here. *Legal competency* relates to the decision of a judge or other legal professional concerning whether or not an individual has capacity under law to carry out a specific act or set of activities.

Accordingly, we disagree with Dr. Cranston that use of the term "competency to consent" in the recent article perpetuates a conceptual error.¹ Rather, use of the term "competency to consent" recognizes that in the medical setting, physicians, psychologists, and other clinicians are called upon to make specific judgments in individual cases as to whether a patient can consent to or can refuse treatment. This consent issue presents as, and is, a decision-specific issue of *competency*, albeit arising in a clinical setting. In arriving at a competency judgment, the clinician may use methods such as clinical interview, treatment consent capacity measures,^{8,11} and as appropriate, neuropsychologic testing^{10,12} to evaluate the individual's *decisional capacity*. Using this information, the clinician makes a judgment of the individual's *competency* to consent to a particular treatment. In many, if not most, instances the competency matter will end there. In some cases, the consent to treatment issue will be presented to the legal system, and a judge will make a judgment of *legal competency*. This legal judgment will be based on a variety of factors, including legal precedent and principles of justice/fairness as well as the clinician's judgment and reasoning.

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