

Temozolomide for Glioblastoma Benefits Elderly

BY KATE JOHNSON

FROM THE ANNUAL MEETING OF THE SOCIETY FOR NEURO-ONCOLOGY

MONTREAL – Elderly patients with newly diagnosed glioblastoma and poor Karnofsky performance scores can benefit from postsurgical chemotherapy with temozolomide, based on the results of a single-arm study in 70 patients.

Most patients were able to withstand treatment-related toxicity, and survival rates and performance status appeared to improve with treatment, Dr. Jamie Gállego Pérez-Larraya said at the meeting.

Median overall survival, the primary end point, reached 25 weeks, with a 6-month overall survival rate of 44.3% and a 12-month rate of 11.4%, said Dr. Pérez-Larraya of Hôpital Pitié-Salpêtrière in Paris. Median progression-free survival, a secondary end point, was 16 weeks, with a 6-month rate of 30%. “These data compare favorably to the 17-week median survival reported in elderly patients with glioblastoma and good performance treated only with palliative care,” he said.

The trial from ANOCEF (Association des Neuro-Oncologues d’Expression Française) enrolled 70 patients aged 70 and up (median age, 77 years), with newly diagnosed and histologically confirmed glioblastoma, a median Karnofsky performance score of 60, and no previous radiotherapy or chemotherapy for the brain tumor. Most (92%) had undergone biopsy of their tumor; five patients had received a partial resection, and one had a complete resection.

VITALS

Major Finding: More than half of patients with a median Karnofsky performance score of 60 improved their score by at least 10 points.

Data Source: A group of 70 elderly, poor-performance patients, treated with postsurgical temozolomide for newly diagnosed glioblastoma.

Disclosures: Dr. Pérez-Larraya reported having no relevant financial disclosures.

Temozolomide chemotherapy started at 150 mg/m² for 5 consecutive days every 28 days, with dose escalation up to 200 mg/m² in the absence of grade 3 or 4 toxicities for a maximum of 12 cycles, or until disease progression. Patients who progressed received supportive care; no radiotherapy was given.

Quality of life (QOL) and cognitive function outcomes were measured by EORTC (European Organisation for Research and Treatment of Cancer) questionnaires (QLQ-C30 and QLQ-BN20), and the Mini-Mental State Examination. The study showed significant improvements on the global QOL scale and most functioning domains, with no decline in any domain, he said.

A third of the cohort improved in Karnofsky performance scores by at least 10 points, and 26% achieved a score of 70 or greater. “This is clinically significant because it means they became capable of self-care,” he noted.

Treatment with temozolomide was “generally well tolerated,” Dr. Pérez-Larraya reported. Twelve patients, (17%) had

grade 3 or 4 thrombocytopenia or neutropenia, but these toxicities did not lead to dose delays or dose reductions. All of the cohort had died by the time of presentation – 87% as a result of disease progression, and 13% from other causes, with no deaths due to toxicity.

“Until a few years ago the treatment of these patients received little attention mainly because of their poor expected survival, but also because of the fear of treatment-related toxicity,” said Dr. Pérez-Larraya. Now patients with good performance scores can be treated with postsurgical radiotherapy, which has been shown to prolong survival from 17 weeks to 29 weeks with-

out causing deterioration in QOL or cognitive function (N. Engl. J. Med. 2007;356:1527-35). But management of patients with poor scores has never been studied, he said. “Radiotherapy requires many trips to the hospital, and increasing fatigue makes this difficult for these severely impaired patients with such a short expected survival,” he said.

The results suggest that temozolomide in elderly patients with glioblastoma and poor performance scores “has an acceptable safety profile; is associated with an improvement in functional status in one-third of cases, and quality of life before progression; and seems to increase survival as compared to supportive care alone,” Dr. Pérez-Larraya concluded. ■

Therapeutic Nihilism Unnecessary

This study clearly shows the acceptable toxicity and benefit of temozolomide in the treatment of elderly patients with low performance scores who received this drug after surgery for newly diagnosed glioblastoma. Temozolomide appeared to improve both survival rates and performance.

The findings highlight the need to get rid of the nihilistic approach toward this population, all too frequently relegated to

hospice without any attempt at therapy. The toxicity was small and the benefits were real, a lesson all physicians caring for the elderly with glioblastoma should remember.



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VIEW ON THE NEWS

New Drugs Deter Progression in Recurrent Meningioma

BY KATE JOHNSON

FROM THE ANNUAL MEETING OF THE SOCIETY FOR NEURO-ONCOLOGY

MONTREAL – The tyrosine kinase inhibitors vatalanib and sunitinib may offer alternative approaches to treating patients with recurrent, high-grade meningioma who have failed surgery and radiation therapy, according to two separate phase II studies.

Both drugs significantly improved survival compared with what is generally expected in this patient population, most of whom had grade II or III tumors. Progression-free survival at 6 months occurred in 57% of 25 patients with meningioma who received the investigational drug vatalanib in one study, and in 36% of 36 patients who received sunitinib in another study. Both drugs are inhibitors of receptors for vascular endothelial growth factor and platelet-derived growth factor.

Sunitinib is marketed under the brand name Sutent and has

been approved by the Food and Drug Administration for the treatment of advanced renal cell carcinoma and gastrointestinal stromal tumor after disease progression on – or intolerance to – imatinib mesylate (Gleevec).

Progression-free survival (PFS) for patients with recurrent grade II and III tumors is usually considered to occur in fewer than 5%, said Dr. Jeffrey Raizer, who presented the vatalanib study at the meeting.

“For recurrence of meningioma, treatment options are limited once patients have failed surgery and radiation, and chemotherapies have been very limited to date,” said Dr. Raizer, director of medical neuro-oncology at the cancer center of Northwestern University and Northwestern Memorial Hospital, both in Chicago.

Despite the encouraging findings of the two studies, a lack of

information on the natural history of these tumors makes it difficult to interpret the studies, said Dr. Michael Vogelbaum, who chaired the session in which the studies were presented.

“While the studies suggest there may be some promise, we

VITALS

Major Finding: Two phase II studies of vatalanib and sunitinib showed 6-month progression-free survival rates of 57% and 36%, respectively.

Data Source: Two cohorts of 25 and 36 patients with recurrent grade II and III meningiomas.

Disclosures: Pfizer funded the study on its drug, sunitinib, and Novartis funded the study on its investigational drug, vatalanib. The investigators did not provide financial disclosure information at the meeting and did not respond to inquiries about disclosures.

don’t really know what to expect from that mix of grade II and III tumors on their own,” Dr. Vogelbaum said in an interview. He is chair of neuro-oncology at the Cleveland Clinic Neurological Institute.

Dr. Fred Barker of the de-

partment of neurosurgery at Massachusetts General Hospital, Boston, echoed Dr. Vogelbaum’s comments. “The results are interesting, but we don’t know exactly what the natural history would be without treatment, so whether there’s a benefit to giving these

drugs will require further study.”

In Dr. Raizer’s Pfizer-sponsored study of vatalanib in meningioma patients, the median PFS was 5.9 months, and the median overall survival was 22.3 months. Of the 25 patients in the study, 22 had grade II and III tumors and 14 were men. The PFS at 6 months was

comparable between patients with grade II (39%) or grade III disease only (43%).

Dosing of vatalanib began at 250 mg twice daily and rose by 250 mg/day every 7 days until it reached 500 mg twice daily.

For 21 patients with available

imaging data, tumors partially responded to treatment in 1, remained stable in 15, and progressed in 5 patients.

The most common adverse events were fatigue, rash, and elevated transaminases.

The sunitinib study, sponsored by Novartis, included 36 patients (median age, 62 years) with recurrent grade II and III meningiomas who had exhausted all surgical and radiation options. The patients had a median of five recurrences.

The primary end point of PFS at 6 months was 36% and the median PFS was 5.1 months. The overall survival rate is not known, as only eight patients have died, reported Dr. Thomas Kaley, codirector of the neuro-oncology fellowship program at Memorial Sloan-Kettering Cancer Center in New York.

Imaging was available for 34 patients and showed stable disease in 26, a partial response in 1, and progressive disease in 7 patients, he said. The dose of sunitinib was 50 mg/day orally on a 4-week-on, 2-week-off cycle. ■