Device Offers Effective Alternative to Chemo

BY SUSAN LONDON

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY

CHICAGO — Treatment with electric fields that disrupt tumor cell processes appears to be at least as effective as the best standard chemotherapy for recurrent glioblastoma and is safe and well tolerated, according to the results of a randomized, open-label, phase III trial.

In the study of 237 patients with recurrent glioblastoma, some of whom were heavily pretreated, median overall survival was 6.6 months among those assigned to treatment with NovoTTF-100A, an investigational device that delivers low-amplitude alternating electric fields through noninvasive, disposable electrodes applied to the shaved head. Among those treated with the standard chemotherapy selected by their physicians, median survival was 6.0 months.

The effects of NovoTTF-100A may not become apparent on MR imaging scans for at least several months.

DR. STUPP

The main adverse event associated with NovoTTF-100A use was mild to moderate skin irritation related to the electrodes in 17% of patients, whereas patients treated with chemotherapy had higher rates of grade 3/4 hematologic adverse events and gastrointestinal adverse events.

"We were afraid that we would...induce seizures with this device," commented lead investigator Dr. Roger Stupp, an oncologist at the University of Lausanne (Switzerland) Hospitals. But "actually, there was no increase in seizure frequency in the patients who got the NovoTTF."

VITALS

Major Finding: Median overall survival in patients having recurrent glioblastoma was 6.6 months with NovoTTF vs. 6.0 months with best standard chemotherapy, and NovoTTF had minimal adverse effects.

Data Source: A randomized, open-label phase III trial (the EF11 trial) among 237 patients with recurrent glioblastoma.

Disclosures: Some of the investigators were employees of, owned stock in, or received research funding from NovoCure, the manufacturer of NovoTTF.

Dr. Stupp explained that the device, which is powered through a portable battery pack, "should generate forces that will disrupt and interfere with cell division and assembly of organelles, either directly or by indirect mechanisms."

Adult patients in the United States, Europe, and Israel were eligible for the trial, called EF-11, if they had recurrent glioblastoma and a good performance status. There was no limitation on the number of prior therapies, and previous surgery for the recurrence was also allowed.

In all, 120 patients were randomized to NovoTTF, with a target of at least 20 hours of use daily, while 117 patients were randomized to best standard chemotherapy at their physician's discretion. All underwent magnetic resonance imaging every 2 months.

The patients had a median age of 54 years, and 70% were men. The median time from initial glioblastoma diagnosis was 11 months.

On average, the patients had received two prior lines of chemotherapy (range, one to five), and 26% had had surgery for their recurrence. Overall, 53% were being treated for a second or third recurrence.

Fully 78% of patients in the NovoTTF group were treated per protocol, defined as having received a dose intensity of at least 70% of that planned during the first month, Dr. Stupp reported. The median daily duration of use was 20 hours.

Similarly, 79% of patients in the chemotherapy group were treated per protocol. The chemotherapies were most often nitrosoureas, PCV (procarbazine, lomustine, and vincristine), or procarbazine (33%); bevacizumab with or without other agents (13%); platinum-based therapy (11%); and temozolomide (11%).

In an intent-to-treat analysis, median overall survival—the trial's primary efficacy end point—was 6.6 months with NovoTTF and 6.0 months with chemotherapy. The 1-year rate of survival was 23.6% vs. 20.7%, respectively, a statistically nonsignificant difference.

However, in a per-protocol analysis, median overall survival was 7.8 months with NovoTTF and 6.1 months with chemotherapy. The 1-year rate of survival in this case was 29.5% vs.19.1%, respectively (hazard ratio, 0.64; $P = .01$).

Similarly, the 6-month rate of progression-free survival did not differ significantly between groups on an intent-to-treat basis (24% vs. 17%), but was twice as high in the NovoTTF group on a per-protocol basis (28% vs. 14%, $P = .04$), according to Dr. Stupp.

He cautioned that the effects of NovoTTF may not become apparent on scans for at least several months. ■

MY TAKE

Option for Failed, Intolerable Chemo

This study is intriguing because it potentially offers our patients a novel therapy with improved tolerability compared to chemotherapy. Once patients with recurrent glioblastoma have had tumor progression in spite of bevacizumab, treatment options are limited. The per-protocol data analysis was most compelling with a statistically significant overall survival of 7.8 months and 1-year survival of 29.5% with the use of the NovoTTF-100A, compared with 6.1 months and 19.1% in the chemotherapy arm.

Imaging was performed in 2-month intervals, and Dr. Stupp alludes to the fact that tumor regression may not be seen on MRI for several months. Therefore, adequate treatment time must be allowed prior to abandoning therapy. One must assume from this statement that the imaging was revealing for tumor stability rather than progression followed by regression. I question whether or not the device has any adverse radiographic effects comparable to radiation necrosis that improves over time. NovoTTF-100A is a promising therapy for patients with recurrent glioblastoma and is an exciting option for patients in whom chemotherapy has failed and or has been intolerable.

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Less Joint Decision Making Reported for Pediatric Tumors

BY CAROLINE HELWICK

FROM THE ANNUAL MEETING OF THE AMERICAN PSYCHO-ONCOLOGY SOCIETY

NEW ORLEANS — For the treatment of pediatric brain cancer, more than 25% of radiation oncologists said they would not expect parents to partake in decision making for scenarios with a high risk for neurocognitive impairment, according to a study by Dr. Robert Olson, a resident in radiation oncology at the University of British Columbia in Vancouver.

"Cure rates for pediatric cancers have risen, but at the cost of increased late effects. Historically, physicians have decided on the trade-off between cure and late effects. More recently, patients' right to choose their own risk/benefit ratio has been accepted in adult oncology, but it is less accepted in pediatric oncology, and oncologists' views about joint decision making have not been well evaluated," Dr. Olson said at the meeting.

The survey, developed by the British Columbia Cancer Agency, collected demographic information, practice patterns, and views on informed consent and joint decision making from 56 oncologists, 84% of whom were radiation oncologists. They primarily practiced in the United States (39%), Canada (30%), and Europe (25%), for a mean of 19 years.

Shared decision making was defined as a process in which the patient and the clinician share information with each other, take steps to participate in the process, and agree on a course of action. Patients can delegate the decision to the physician, but would share in the discussion first, Dr. Olson noted.

Several hypothetical cases were presented to illustrate the difficulty in quantifying the risk/benefit ratio and the complexity of discussions.

The first case involved a 5-year-old boy with metastatic medulloblastoma to the craniospinal axis for which radiation treatment would likely cause severe cognitive impairment. In this scenario, 100% of respondents said they would discuss cognitive side effects with the parents, and 84% said they would find these discussions stressful. The more complicated scenario was case number two, involving a 4-year-old boy with a completely excised medulloblastoma that was confined to the posterior fossa. The treatment choices were radiotherapy with minimally intense chemotherapy, which offered an 80%-90% chance of cure but a high risk of neurocognitive impairment, and high-dose chemotherapy with stem cell rescue, which offered a 40%-70% chance of cure but a low risk for neurocognitive impairment. For treatment, 84% of respondents chose radiotherapy, which could be partly explained by the fact that most responders were radiation oncologists.

For this scenario, 72% of respondents indicated that there was a role for joint decision making with parents, whereas 23% felt there was not. Their answers did not differ significantly according to age, sex, country, years in practice, time spent with patients, and number of new patients per year.

The oncologists' comments for this scenario included: "Parents must have a say and a choice of treatment"; "Clinicians should guide but not burden the parents to decide"; and "It is important not to make the parents the final deciders, as they may well carry significant guilt if there are adverse outcomes."

"It is worrisome that only [three-quarters or less] of oncologists feel that parents should have a say in these treatment decisions," Dr. Olson remarked, "but, still, there has been a shift toward shared decision making compared to a time when parents were not often given a say at all." ■