

Preop Depression Linked to Shorter Brain Tumor Survival

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Patients suffering from depression at the time of malignant brain astrocytoma surgery had significantly reduced survival compared with nondepressed patients in a retrospective analysis of 1,052 patients.

Although no causative association can be inferred because of the study's retrospective design, recognizing and treating preoperative depression could maximize survival in patients with malignant brain tumors, Dr. Alfredo Quiñones-Hinojosa said at the annual meeting of the American Association of Neurological Surgeons.

Currently, patient age, tumor grade, and functional status are known preoperative prognostic indicators of survival. Identification of any reversible comorbidity would be important, as malignant astrocytoma, also known as glioma or glioblastoma multiforme, typically results in death in about 1 year, even with the latest, most effective therapies.

Researchers at Johns Hopkins University in Baltimore, led by Dr. Matthew J. McGirt, analyzed the outcomes of 1,052 patients with malignant astrocytoma who underwent surgery from 1995 to 2006.

Of these patients, 605 underwent primary resection, 410 underwent secondary resection, and 37 had a biopsy only. Excluding the biopsies, 213 tumors were World Health Organization grade III and 802 tumors were grade IV.

A total of 204 patients received subtotal resection, 274 received adjuvant therapy, and 136 required subsequent resection.

Only 49 patients (5%) who were found to be taking antidepressant medication for clinical depression at the time they underwent surgery

met the study's definition of having depression. All demographic and clinical characteristics were similar between the two groups, said Dr. Quiñones-Hinojosa. Their mean age was 51 years and median preoperative Karnofsky Performance Scale (KPS) score was 80. Among survivors, the median follow-up was 12 months (range 3-18 months).

In a Kaplan Meier analysis, patients with depression had more than a 40% increase in the relative risk of mortality compared with nondepressed patients (relative risk 1.41), regardless of KPS, WHO tumor grade, patient age, or clinical presentation. This association was independent of extent of resection and postoperative treatment with either adjuvant temozolomide chemotherapy or Gliadel wafer use, Dr. Quiñones-Hinojosa said.

Median survival was 7 months among patients with depression, vs. 11 months in those without depression.

At 2 years post surgery, 5% of patients with depression were alive, compared with 23% of nondepressed patients. The difference was significant, he said.

Dr. Quiñones-Hinojosa acknowledged that the investigators could not be certain that the patients' depression was not a response to the recent diagnosis of a terminal disease. In addition, many patients with clinical depression may have been undiagnosed and unmedicated, lowering the sensitivity of the classification scheme.

Discussant Stephen B. Tatter, a neurosurgery professor at Wake Forest University, Winston-Salem, N.C., said treating depression in this patient population is important as it might influence a variety of patient decisions, particularly when to stop treatment. "We don't want just to prolong life but to provide quality that is acceptable to patients," Dr. Tatter said. ■

Modafinil Reduced Severe Fatigue in Cancer Patients

BY KERRI WACHTER
Senior Writer

CHICAGO — The wakefulness-promoting drug modafinil (marketed as Provigil) reduced self-reported severe fatigue, according to a recent study of more than 600 cancer patients who were undergoing chemotherapy.

Gary R. Morrow, Ph.D., of the University of Rochester (N.Y.) and his colleagues randomized 631 patients undergoing four cycles of chemotherapy to receive either 200 mg modafinil daily or placebo. Among those with severe fatigue at baseline, patients on modafinil had significantly greater reductions in fatigue, compared with those on placebo.

Dr. Morrow presented his study's findings at the annual meeting of the American Society of Clinical Oncology.

Study participants were asked to rate their level of fatigue at baseline (during the second cycle of chemotherapy) and during the final cycle.

They rated fatigue on a 10-point scale: mild (1-4), moderate (5-6), and severe (7-10).

A total of 67 patients reported mild fatigue at baseline; 106 and 458 reported moderate and severe fatigue, respectively.

Among patients with mild and moderate fatigue, modafinil also reduced fatigue, compared with

placebo, but the differences were not significant.

This was not surprising, Dr. Morrow commented during a press briefing.

"With side effects, quite often the potency of the effect is somewhat dependent on where you began," he said.

Modafinil—a nonamphetamine stimulant—is currently indicated for the treatment of excessive sleepiness resulting from obstructive sleep apnea, shift-work sleep disorder, and narcolepsy. Last year, researchers also at the University of Rochester reported success with modafinil in treating "chemobrain," a reduction in cognitive function that has been associated with chemotherapy.

There may be some overlap between chemobrain and fatigue, Dr. Morrow said in an interview. Problems with executive function are commonly described in chemobrain.

Cancer-related fatigue appears to particularly affect tasks associated with executive function.

Cancer patients complain of not being able to "get around" to doing things they know they should do.

The pharmaceutical company Cephalon Inc. provided modafinil and placebo for the trial.

Dr. Morrow reported that he has no relevant financial relationships to disclose. ■

No Evidence of 'Chemobrain' in Small Breast Cancer Cohort

BY DENISE NAPOLI
Assistant Editor

CHICAGO — Chemotherapy-related cognitive impairment was infrequent in a small study of 30 patients who underwent adjuvant chemotherapy for non-metastatic breast cancer.

"People could be making decisions about whether or not to have chemotherapy based on stories they've heard about 'chemofog' or 'chemobrain,'" according to Dr. David G. Darby. "We hope this information will help people make informed decisions."

Dr. Darby and his colleagues looked at a total of 30 women who had already undergone either lumpectomy or mastectomy and were scheduled to undergo either the chemotherapy regimen known as AC (n = 15) or CEF or CMF regimens (n = 15).

► The AC regimen involves doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m² intravenously, repeated every 21 days for a total of four cycles.

► The CEF regimen involves cyclophosphamide administered orally in doses of 75 mg/m² on days 1-14; epirubicin 60 mg/m² by IV on days 1 and 8; and 5-fluorouracil 500 mg/m² by IV on days 1 and 8, repeated every 28 days for six cycles.

► The CMF regimen involves cyclophosphamide 100 mg/m² given orally on days 1-14; methotrexate in doses of 40 mg/m² IV on days 1 and 8; and 5-fluorouracil 600 mg/m² IV on days 1 and 8, repeated every 28 days for a total of six cycles.

The women were compared with 30 age-matched controls.

Women took several tests designed to measure cognition as well as mood a few days before initiating chemotherapy (but after the diagnosis had been given and treatment course was decided); again at the start of each new treatment cycle; and for the last time 28 days after the final treatment cycle had begun in each group. Patients were assessed on the National Institute of Mental

Health's Center for Epidemiologic Studies Depression Scale (CES-D) depression, the state trait anxiety inventory (STAI) scale, and a test of Dr. Darby's own design, which measures detection speed, identification speed, working memory, and learning ability in a 10- to 12-minute battery.

Dr. Darby is the chief medical officer of a company he formed, called CogState, which produces and scores these tests. It is based in Australia and partly funded this study.

"The first finding of interest was that prior to the first cycle of chemo there was impairment in learning of moderate amplitude, and that was also associated with a mild reduction on mood scales or depressive scales," said Dr. Darby in an interview. No women were clinically depressed (clinically depressed patients were excluded from the study) and none of the women was on antidepressants at baseline or throughout the study. However, "there

may have been an impairment there initially, prior to chemo."

Two other findings also emerged, both good and bad. "There was an improvement of some of the learning aspects of their performance and a mild improvement on scores on anxiety scales, but there was also a mild deterioration in aspects of concentration and psychomotor speed [as the study progressed]." There was also evidence that patients' mood was declining slightly throughout the treatment.

Individual patients showed "quite a lot of variation—in particular, some patients would have impairment on only one occasion and then improve, and others would have impairment on two or more occasions," he said. Persistent impairment, that occurring on two consecutive occasions, was seen in only three patients, or 10% of the total, Dr. Darby reported at the annual meeting of the American Academy of Neurology.

Impairment in concentration

was not severe, "equivalent to the sort of jet-lag that I'm feeling now, having traveled from Australia." He also likened it to the sort of impairment one would feel after being awake for about 17 hours.

Dr. Darby found no significant differences in the risk for cognitive impairment based on the women's age, menopausal status (pre-, peri-, or post-), or time from surgery.

"When women are confronting breast cancer, coming to terms with the many different aspects of it, and trying to take advice and understand what's happening to them, the issues of quality of life are important. They should realize that these sorts of changes seem to be very mild. They are present in a minority of women, and they can be measured as well, if need be. In general, discussion with the patients about the mildness of these sorts of changes is probably the most appropriate [course for the treating physician]," said Dr. Darby. ■