BRAIN

Tumor Characteristics May Help Predict Prognosis in Patients with Oligodendroglioma

Group: Radiation Therapy Oncology Group; the European Organisation for Research and Treatment of Cancer

A large phase III study (RTOG-9402) in patients with anaplastic oligodendroglioma comparing chemotherapy and radiotherapy vs. radiotherapy alone found that a subset of patients with a particular genetic profile experienced better overall survival, regardless of what treatment they received. Oligodendroglioma is a type of glioma normally found in the cerebrum, particularly in the frontal or temporal lobes. The tumor is most common in adults and occurs more often in men than in women. Researchers found that patients receiving chemotherapy plus radiotherapy did not live significantly longer than patients who received radiotherapy alone. In a secondary finding, researchers discovered that patients whose tumors lacked the 1p and 19q alleles (46% of patients) had significantly longer median survival times than those with intact 1p and 19q alleles (7.0 vs. 2.8 years, respectively), indicating that tumors with this genetic profile may be less aggressive, more responsive to therapy, or both. (An allele is an alternative form of a gene.) This trial\(^1\), and another large phase III trial in the same patient population (EORTC 26951)\(^2\) were the first large studies to validate a link between 1p/19q deletions and patient outcome. Based on these findings, it is no longer rational to treat these patients according to histologic classification alone without taking the genotype of these tumors into account.

BREAST

Trastuzumab (Herceptin) Cuts Breast Cancer Recurrence in Half, Increases Survival.

Group: National Surgical Adjuvant Breast and Bowel Project; North Central Cancer Treatment Group

Trastuzumab, which targets and blocks a protein called HER-2, has been used since 1998 to treat breast cancer that has returned after surgery, or that has spread to other parts of the body. A combined analysis of two large cooperative group trials, NSABP B-31 and NCCTG N9831, indicates that trastuzumab can also be extremely effective if used earlier in the course of treatment, immediately following surgery, to prevent recurrence. The findings represent a very

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significant advance in breast cancer treatment, and will change the care of the 25% to 30% of breast cancer patients whose tumors contain excessive amounts of the HER-2 protein. The protein is associated with an increased risk of cancer recurrence and a decreased sensitivity to chemotherapy. The cooperative group analysis showed for the first time that adding trastuzumab to standard chemotherapy for early-stage breast cancer that overexpress HER-2 reduced the risk of recurrence in women by 52% after three years compared with chemotherapy alone. In addition, women who received trastuzumab as part of their therapy had a 33% lower risk of death after three years; three-year survival rates were 94.3% for the women who received trastuzumab, compared with 91.7% of those who received chemotherapy alone.

**Bevacizumab (Avastin) Slows Cancer Growth.**
*Group:* Eastern Cooperative Oncology Group

Bevacizumab, which is approved for treating advanced colorectal cancer, may also have a role in the treatment of breast cancer. Study E2100 showed that adding bevacizumab to the standard chemotherapy drug paclitaxel (Taxol) nearly doubled the time it took for cancer to grow in women whose breast cancer had returned or spread to other parts of the body, compared with women who received paclitaxel alone.

**Tamoxifen and Raloxifene are Equally Effective in reducing the risk of developing Invasive Breast Cancer, but Differences Seen for Non-Invasive Breast Cancer, Side Effects.**
*Group:* National Surgical Adjuvant Breast and Bowel Project

Findings from one of the largest breast cancer prevention trials ever conducted – the Study of Tamoxifen and Raloxifene (STAR) – showed that tamoxifen and raloxifene were equally effective in preventing invasive breast cancer in women at high risk for the disease, reducing risk by about 50%. The study also found that raloxifene was not as effective as tamoxifen in the reduction of non-invasive breast cancer, but that tamoxifen caused more uterine cancers and blood clots than raloxifene. The findings underscore the need for women and their physicians to consider a woman’s medical history, current symptoms, and personal preferences when choosing between therapies. Tamoxifen is approved by the FDA for three purposes—to treat metastatic breast cancer, to reduce the risk of breast cancer recurrence and to reduce the risk of developing the disease in both pre- and post-menopausal women at high risk for breast cancer. Raloxifene is approved to prevent osteoporosis, and has also been shown in previous clinical trials to reduce breast cancer risk in postmenopausal women.

**CHILDHOOD CANCER SURVIVORS**

**Many Childhood Cancer Survivors Have Significant Health Problems as Adults.**
*Group:* Childhood Cancer Survivor Study Group

The Childhood Cancer Survivor Study surveyed more than 10,000 adult survivors of childhood cancers treated in the 1970s and 1980s, finding that the risk of having a moderate to severe health problem was five times greater for survivors, compared with their healthy siblings. The study provides the first estimate of the frequency of health problems in childhood cancer survivors as they become adults, and supports the need for greatly enhanced, long-term follow-up medical care for these individuals. It also highlights the need for additional research to develop less toxic treatment approaches that do not kill efficacy. Researchers measured the incidence of moderate and severe chronic health problems, finding that by age 45, 57.1% of the survivors and 18.2% of the siblings reported a moderate health problem; 37% of survivors and 4.6% of the siblings reported severe health problems. The relative risk of a survivor having a grade 3 or 4 chronic disease was 5 times greater when compared with their siblings. Examples of health problems included second cancers, heart disease, and scarring of the lungs.
**COLORECTAL**

**Oxaliplatin-containing Chemotherapy Becomes Part of Standard Care for Colorectal Cancer.**

**Groups:** National Surgical Adjuvant Breast and Bowel Project, Eastern Cooperative Oncology Group

Several important recent studies demonstrated the value of a chemotherapy regimen called FOLFOX—which combines the anticancer drugs oxaliplatin (Eloxatin), 5-fluorouracil (5FU), and leucovorin (LV)—in reducing the risk of colorectal cancer recurrence. Coupled with similar data from previous studies, these findings have changed the treatment approach for patients with early-stage colorectal cancer who need chemotherapy after surgery. One large international study—the MOSAIC trial, sponsored by Sanofi-Synthelabo, found that adding oxaliplatin to standard chemotherapy after surgery for early-stage colorectal cancer reduced the risk of recurrence by 24%. A separate study by researchers from the NSABP (C-07) showed that adding oxaliplatin to standard chemotherapy reduced the risk of recurrence by 21% in early-stage colorectal cancer patients. An additional study in patients with advanced colorectal cancer demonstrated that adding bevacizumab (Avastin) to the FOLFOX regimen could increase survival. Researchers from ECOG (E3200) reported that the regimen improved overall survival by 17% among patients with advanced colorectal cancer who had received previous chemotherapy for metastatic disease. Bevacizumab is currently approved for the initial treatment of advanced colorectal cancer when given in combination with standard chemotherapy.

**LEUKEMIA AND LYMPHOMA**

**FDA Approves Pegaspargase for Newly Diagnosed Acute Lymphoblastic Leukemia.**

**Group:** Childrens Cancer Study Group

In July 2006, the FDA approved pegaspargase (Oncaspar) to treat children newly diagnosed with acute lymphoblastic leukemia (ALL), the most common cancer diagnosed in children. The FDA approval of the drug for use among children was based on a randomized, multicenter trial of 118 pediatric patients, which demonstrated the pegaspargase could be safely used as an alternative to the previous standard of care, L-asparaginase, as part of a multi-drug regimen for ALL. The major advantage of pegaspargase is that it requires significantly fewer injections than L-asparaginase—three injections over a 20-week period, compared with 21 injections for the standard regimen.

**FDA Approves Nelarabine for Rare Leukemia and Lymphoma.**

**Group:** Children’s Oncology Group

In October 2005, the FDA approved nelarabine (Arranon) for the treatment of children with T-cell acute lymphoblastic leukemia (T-ALL) and T-cell lymphoblastic lymphoma (TLBL), whose cancer has not responded to or has returned following two chemotherapy regimens. In a study of 39 pediatric patients with resistant or recurrent T-ALL/T-LBL, 23% experienced complete remission of disease, which lasted from 3.3 to 9.3 weeks. Nelarabine is the first drug approved to treat this limited population of patients.

**Maintenance Rituximab Extends Survival in Advanced Follicular Lymphoma.**

**Group:** Eastern Cooperative Oncology Group

For the first time, a phase III, multi-center trial (E1496) has shown that two years of maintenance therapy with the monoclonal antibody rituximab (Rituxan)—which blocks a specific protein on B-lymphocytes—after completion of convention chemotherapy improved survival and slowed disease progression in patients with advanced follicular lymphoma. Maintenance therapy is
extended drug therapy, usually at a diminished dose, administered after a disease has been brought under control. Four years after beginning treatment, 56% of patients who received maintenance rituximab showed no evidence of cancer growth, compared with 33% of patients who were observed following chemotherapy. Moreover, 88% of the rituximab group was still alive after four years, compared with 72% of the observation group.

LUNG

Bevacizumab (Avastin) Improves Survival in Advanced Lung Cancer.
Group: Eastern Cooperative Oncology Group
A large trial (E4599) demonstrated that the angiogenesis inhibitor bevacizumab in combination with chemotherapy can significantly extend survival in patients with advanced non-squamous cell lung cancer. It is the first time a study has shown that adding a targeted agent to standard chemotherapy increases survival for patients with advanced NSCLC, and is particularly important because nearly two-thirds of patients with metastatic NSCLC are eligible for this regimen. Researchers found that adding bevacizumab to standard combination chemotherapy (paclitaxel and carboplatin) increased survival – patients receiving bevacizumab survived 12.5 months compared with 10.2 months for patients who received standard therapy alone.

Definitive Study Demonstrates Effectiveness of Adjuvant Chemotherapy for Early-stage Lung Cancer.
Groups: National Cancer Institute of Canada Clinical Trials Group and the U.S. National Cancer Institute Intergroup Trial, Cancer and Leukemia Group B
Until now, questions have persisted about the benefit of adjuvant chemotherapy in the treatment NSCLC. The detailed results of a large randomized trial (JBR-10) showed that giving chemotherapy after surgery to patients with early-stage NSCLC significantly extends survival. The study resolves a long standing debate about the benefit of adjuvant chemotherapy, definitively demonstrating that such treatment has a beneficial role in the care of patients with operable NSCLC. Researchers with the NCIC and the U.S. National Cancer Institute Intergroup Trial found that overall survival among patients with early-stage NSCLC who received the anticancer drugs vinorelbine and cisplatin after surgery was 94 months, compared with 73 months for patients who did not receive such adjuvant chemotherapy. Five-year survival was also highest in the chemotherapy group (69% versus 54%), and the risk of recurrence was 40% lower in the chemotherapy group.

These findings, along with those reported recently by the Adjuvant Navelbine International Trialist Association (ANITA) and CALGB for its study, CALGB-9633, confirm that adjuvant chemotherapy has a significant role in the treatment of patients with operable NSCLC who are in otherwise good health.

OVARIAN

Chemotherapy Delivered Into the Abdomen Extends Survival for Women with Advanced Ovarian Cancer.
Group: The Gynecologic Oncology Group (GOG)
A Study conducted by the GOG found that delivering chemotherapy directly into the abdomen (“intraperitoneal” chemotherapy), in addition to intravenous chemotherapy, significantly extended survival in women with advanced ovarian cancer. The phase III trial included 415 patients with advanced ovarian cancer. Researchers found that the addition of intraperitoneal therapy
extended median survival by more than one year (49.7 months vs. 65.6 months) compared with intravenous chemotherapy alone.\textsuperscript{xiv}

PANCREATIC CANCER

No Advantage to Adding Oxaliplatin to Gemcitabine for Pancreatic Cancer.

Group: Eastern Cooperative Oncology Group

A phase III, multi-center trial (E6201) showed that two investigational pancreatic cancer treatments—fixed dose-rate gemcitabine and gemcitabine plus oxaliplatin (GEMOX)—did not improve survival when compared with the current standard of care, a 30-minute infusion of gemcitabine, in patients with advanced, inoperable pancreatic cancer. Because gemcitabine, the standard therapy for pancreatic cancer, offers only a modest survival advantage over no treatment, researchers have been studying a number of new approaches, alone or in combination with gemcitabine, to determine better ways of fighting the disease. This study adds to several previous studies showing that adding another chemotherapy agent to gemcitabine does not provide any advantage over gemcitabine alone.\textsuperscript{xv}

TESTIS

High-Dose Chemotherapy is not Superior to Conventional Chemotherapy in Testis Cancer.

Group: Intergroup trial (ECOG, SWOG, CALGB participation)

A randomized phase III trial comparing high-dose chemotherapy with conventional-dose chemotherapy found that the addition of high-dose therapy did not improve survival or response rates for patients with metastatic germ cell tumors (primarily testis cancer). The study adds to a growing body of evidence showing that high-dose chemotherapy is not superior to conventional dose therapy in a number of cancer types and may be associated with significant risks and additional side effects. \textsuperscript{xvi}

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Bajorin DF, Nichols CR, Margolin KA, et al. Phase III trial of conventional-dose chemotherapy alone or with high-dose chemotherapy for metastatic germ cell (GCT) patients (PTS): A cooperative group trial by Memorial Sloan-Kettering Cancer Center, ECOG, SWOG, and CALGB. J Clin Oncol. 2006;24:18s(abstr 4510).