# Abnormal chromosome indicator of treatment and outcome in patients with rare brain tumor

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A recent analysis of clinical trial results performed by the Radiation Therapy Oncology Group (RTOG) demonstrate that a chromosomal abnormality—specifically, the absence (co-deletion) of chromosomes 1p and 19q—have definitive prognostic and predictive value for managing the treatment of adult patients with pure and mixed anaplastic oligodendrogliomas. The presence of the chromosomal abnormality was associated with a substantially better prognosis and near-doubling of median survival time when treatment with combined chemotherapy and radiation therapy was compared to treatment with radiation therapy alone.

Oligodendrogliomas are uncommon tumors that represent approximately 4.0% of all brain tumors. Mixed oliogdendrogliomas (those also containing astrocytic elements) account for 1.0% of all brain tumors. Pure and mixed oligodendrogliomas that contain anaplastic (malignant) cells typically grow more rapidly than non-anaplastic tumors.

The RTOG 9402 trial A Phase III Intergroup Randomized Comparison of Radiation Alone vs. Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas was conducted with four other National Cancer Institute (NCI)-supported cooperative groups. Trial participants had a pathologically confirmed pure or mixed anaplastic oligodendroglioma and were randomly assigned into one of two treatment arms. The 148 participants randomized to Arm 1 were treated

with PCV (procarbazine, CCNU [lomustine] and vincristine) chemotherapy and radiation therapy (RT), and the 143 participants randomized to Arm 2 were treated with RT alone.

RTOG 9402 study results reported with a minimum follow-up time of 3 years in the *Journal of Clinical Oncology* (2006 Jun 20; 24(18): 2707-14) showed no survival benefit for patients treated with early PVC chemotherapy plus RT over RT alone. Although a significant impact on median progression-free survival time was realized (2.6 years versus 1.7 years for RT alone), the regimen was associated with significantly more adverse side effects. The study authors also reported that study participants in both arms whose tumor lacked chromosomes 1p and 19q had longer median survival times as compared with participants without these deletions (> 7 vs. 2.8 years, respectively). This led the study authors to conclude that "tumors with 1p and 19q co-deletion are less aggressive or more responsive to PCV chemotherapy or both."

A recent analysis undertaken of the RTOG 9402 data (at a median study participant follow-up time of 11 years) is planned for submission to the 2012 American Society of Clinical Oncology Annual Meeting. However, due to the finding's significance for patient care, results are reported here in advance of submission.

The abstract reports that the 126 study participants with 1p and 19q co-deletion, the median survival time (MST) of 59 participants randomized to the PCV chemotherapy and RT arm was much longer than the 67 participants randomized to the RT alone arm (14.7 years vs. 7.3 years). Interestingly, for study participants whose tumors contained only one deletion (either 1p or 19q) or no deletions, no difference was found in MST between the two treatment arms (2.6 years vs. 2.7 years).

"The profound association between improved outcome for patients who lack the 1p and 19q chromosomes and were treated with PCV

chemotherapy and radiation therapy has significant implication for patients with anaplastic oligodendrogliomas. We now have unequivocal evidence that the chromosomal structure of 1p and 19q co-deletion can be used as a marker to determine which patients will benefit from combined chemotherapy and radiation therapy" says the principal investigator for the RTOG 9402 trial and the abstract's primary author J. Gregory Cairncross, MD, Professor and Head of the Department of Clinical Neurosciences at the University of Calgary, Alberta, Canada.

The other NCI-supported cooperative groups participating in the intergroup (INT 0149) trial are the Eastern Oncology Cooperative Group, SWOG, North Central Cancer Treatment Group, and the NCIC Clinical Trials Group.

"These are exciting and practice-changing results," says Walter J. Curran, Jr., MD, RTOG Group Chair and Executive Director of the Winship Cancer Institute of Emory University in Atlanta. "Given the low incidence of this disease, this achievement required the close collaboration of many groups and centers and everyone associated with the trial should be proud of the accomplishment."

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