EORTC study identifies patients with anaplastic oligodendroglioma that benefit from adjuvant PCV

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A further report on the results of EORTC trial 26951 indicates that CpG island methylator phenotype (CIMP) status and O 6-methylguanine-DNA methyltransferase (MGMT) promoter methylation as assessed by MGMT-STP27 are the most informative for identifying grade III glioma patients who might benefit from the addition of procarbazine, CCNU and vincristine (PCV) chemotherapy to radiation therapy. Prior results had shown that PCV chemotherapy following standard radiation therapy delayed tumor growth and extended the lives of patients with anaplastic oligodendroglial tumors, a hard-to-treat form of brain cancer.

Results observed in the phase III RTOG 9402 trial, in this case with chemotherapy preceding radiation therapy, complemented the results obtained previously in the EORTC 26951 trial and found that administering both PCV and radiation therapy led to comparable improvements in survival for oligodendroglial tumor patients with specific deletions of genetic material in chromosomes 1p and 19q, but not for patients without the mutation.

Nevertheless up to 30% of oligodendroglial tumors do not have 1p/19q deletion but may still respond to chemotherapy. Analyses of EORTC 26951 and RTOG 9402 suggested that other molecularly defined subsets of grade III tumors might benefit as well.

The new results will be presented at an ASCO 2013 Clinical Science

Symposia on Sunday, 02 June 2013 by Dr. Martin J. Van Den Bent of the Erasmus Medical Centre Cancer Institute, Rotterdam, The Netherlands, and coordinator of the study. According to Dr. Van Den Bent, "This is further evidence pointing towards a central role of methylation in the behavior of IDH (isocitrate dehydrogenase) mutated glioma and, more in general, of the MGMT gene function in glioma when treated with chemotherapy."

Methylation profiles of 115 patients were conducted using Infinium HumanMethylation27 or Infinium HumanMethylation450 BeadChip kits. (Validation in an independent dataset is required.)

In these analyses, two markers, CIMP and MGMT-STP27 methylation status, were considered promising in being able to differentiate between patients who will and will not respond to PCV chemotherapy. Two other markers, IDH mutation status and 1p/19 chromosomal deletion, had less strength in achieving this differentiation.

The EORTC 26951 intergroup trial was coordinated by the EORTC Brain Tumor Group in collaboration with the Medical Research Council Clinical Trial Unit and supported by Stichting STOPhersentumor.nl. This academic trial was activated in August 1996, closed in March 2002, and included 368 patients in 40 sites in 10 countries: Austria, Belgium, Finland, France, Germany, Hungary, Italy, Sweden, The Netherlands, and the United Kingdom.

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