Personalized care in neuro-oncology coming of age: why we need MGMT and 1p/19q testing for malignant glioma patients in clinical practice.


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Abstract

Histological subtyping and grading by malignancy are the cornerstones of the World Health Organization (WHO) classification of tumors of the central nervous system. They shall provide clinicians with guidance as to the course of disease to be expected and the choices of treatment to be made. Nonetheless, patients with histologically identical tumors may have very different outcomes, notably in patients with astrocytic and oligodendroglial gliomas of WHO grades II and III. In gliomas of adulthood, 3 molecular markers have undergone extensive studies in recent years: 1p/19q chromosomal codeletion, O(6)-methylguanine methyltransferase (MGMT) promoter methylation, and mutations of isocitrate dehydrogenase (IDH) 1 and 2. However, the assessment of these molecular markers has so far not been implemented in clinical routine because of the lack of therapeutic implications. In fact, these markers were considered to be prognostic irrespective of whether patients were receiving radiotherapy (RT), chemotherapy, or both (1p/19q, IDH1/2), or of limited value because testing is too complex and no chemotherapy alternative to temozolomide was available (MGMT). In 2012, this situation has changed: long-term follow-up of the Radiation Therapy Oncology Group 9402 and European Organisation for Research and Treatment of Cancer 26951 trials demonstrated an overall survival benefit from the addition to RT of chemotherapy with procarbazine/CCNU/vincristine confined to patients with anaplastic oligodendroglial tumors with (vs without) 1p/19q codeletion. Furthermore, in elderly glioblastoma patients, the NOA-08 and the Nordic trial of RT alone versus temozolomide alone demonstrated a profound impact of MGMT promoter methylation on outcome by therapy and thus established MGMT as a predictive biomarker in this patient population. These recent results call for the routine implementation of 1p/19q and MGMT testing at least in subpopulations of malignant glioma patients and represent an encouraging step toward the development of personalized therapeutic approaches in neuro-oncology.