**Perspective**

**Epidermal Growth Factor Receptor Inhibitors in Neuro-oncology: Hopes and Disappointments**

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Despite advances in diagnosis and treatment made over the past two decades, high-grade gliomas are still incurable neoplasms. Moreover, after failing adjuvant therapy, few active treatments are available. In this setting, novel agents, such as new chemotherapy compounds and anticancer agents against specific molecular targets, have therefore been investigated. Epidermal growth factor receptor (EGFR) is an intriguing target in high-grade gliomas because it is frequently overexpressed due to amplification of the *EGFR* gene. Gefitinib and erlotinib act as ATP mimetic agents, binding to the cytoplasmic ATP pocket domain and blocking receptor phosphorylations and, thereby, EGFR-mediated activation of downstream pathways. These drugs have been evaluated in several clinical trials treating recurrent high-grade gliomas with contrasting results. Retrospective correlative analyses generated a plethora of putative predictive factors of activity of EGFR tyrosine kinase inhibitors. The first generations of studies on EGFR inhibitors have not found significant activity of...
these agents in high-grade gliomas. Furthermore, no clear molecular or clinical predictors have been identified. As with other targeted agents, prospective trials using specific criteria and standardized methods to evaluate tissue biomarkers are required to find predictors of EGFR inhibitors activity in high-grade glioma patients.