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Molecularly targeted therapy and radiogenomic imaging in glioblastoma

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Glioblastoma (WHO grade IV) is the most common malignant primary brain tumor in adults with a dismal median overall survival of 16 months, despite intensive radio-chemotherapy. In recent years, the advent of high-throughput genomic analyses has helped us to better understand the biology underlying this disease. These advances translate in two ways “from bench to bedside”: First, tumors now can robustly be grouped in molecularly defined subgroups, which increasingly complement the WHO classification, and even prove to be prognostically superior to it. Secondly, key molecular “driver” alterations and biomarkers predictive of therapy response have been identified and caused a great interest in the development of molecularly targeted therapies in these highly treatment-resistant tumors. Today, treatment decisions are increasingly based on defined molecular biomarkers, most prominently the methylation status of O6-methylguanine-DNA methyltransferase (MGMT) promoter or combined deletion of the short arm of chromosome 1 and the long arm of chromosome 19 (1p/19q codeletion), a hallmark of oligodendroglial tumors. Furthermore, several actionable alterations have been identified which are recurrently found in these tumors, such as isocitrate dehydrogenase (IDH) mutations, epidermal growth factor receptor (EGFR) amplifications or FGFR-TACC fusions. In parallel, fostered by advancements in MR and PET imaging and post-processing, the field of radiogenomics, investigating how genomics are reflected in the imaging phenotype, has received increasing attention. These developments have been met with great enthusiasm, as drugs targeting defined genomic alterations promised to improve therapeutic options for this disastrous disease, while hopefully reducing side effects compared to conventional chemotherapeutic agents.

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