A contemporary perspective on the diagnosis and treatment of diffuse gliomas in adults

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Gliomas are intrinsic brain tumours, which are classified by the World Health Organization (WHO) into different grades of malignancy, with glioblastoma being the most frequent and most malignant subtype (WHO grade IV). Mutations in the isocitrate dehydrogenase (IDH) 1 or 2 genes are frequent in lower (WHO II/III) grade tumours but typically absent in classical glioblastoma. IDH mutations are associated with a better prognosis compared with IDH wild-type tumours of the same WHO grade. Following detection of a tumour mass by imaging, maximum safe surgery as feasible is commonly performed to reduce mass effect and to obtain tissue allowing histopathological diagnosis and molecular assessment. Radiotherapy has been the mainstay in the treatment of diffuse gliomas for several decades. It provides improved local control, but is not curative. Furthermore, several randomised trials have shown that the addition of alkylating chemotherapy, either temozolomide or nitrosourea-based regimens, to radiotherapy results in prolonged survival. Tumour-treating fields (TTFields) have emerged as an additional treatment option in combination with maintenance temozolomide treatment for patients with newly diagnosed glioblastoma. Treatment at recurrence is less standardised and depends on the patient’s performance status, symptom burden and prior treatments. Bevacizumab prolongs progression-free survival in newly diagnosed and recurrent glioblastoma, but does not impact overall survival. However, in Switzerland and some other countries, it is still considered a valuable treatment option to reduce clinical symptom burden. Given the generally poor outcome for these patients, various novel treatment approaches are currently being explored within clinical trials including immunotherapeutic strategies such as immune checkpoint inhibition and the brain-penetrant proteasome inhibitor marizomib.

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