Low-grade glioma chemotherapy

see also Low-grade glioma treatment.

The standard postsurgical options for low-grade gliomas include watchful waiting or radiotherapy depending on the risk factors for recurrence. The use of chemotherapy for the treatment of this disease is generally controversial, although the published results of the first of two large Phase 3 randomized controlled trials (RTOG 9802 a EORTC 22033-26033), focusing on the evaluation of chemotherapy for the upfront treatment of newly diagnosed low-grade gliomas, are reassuring in this respect. The long-term results of a RTOG 9802 comparing radiotherapy alone with radiotherapy and six cycles of adjuvant PCV chemotherapy (procarbazine, lomustine, vincristine) in patients with high risk low-grade gliomas will probably have an impact on daily clinical practice. The increase in median overall survival from 7.8 years to 13.3 years, mainly for patients with oligodendrogliomas, is unprecedented, but the toxicity of PCV is too high and molecular marker analysis remains inadequate. It is still unclear whether less toxic temozolomide can replace PCV and whether temozolomide can be used upfront alone instead of with radiotherapy. This question is addressed by the ongoing EORTC 22033-26033 study. The preliminary results show no significant difference in progression-free survival between patients receiving radiotherapy and those receiving temozolomide alone. Treatment with temozolomide was not associated with an improvement in cognitive function compared with treatment with radiotherapy. Despite limited follow-up, the study clearly confirmed the importance of molecular characterization of low-grade gliomas, defined in the World Health Organization Classification of Tumors of the Central Nervous System 2016 [1)].

The role of chemotherapy in low-grade glioma treatment has been redefined with the long-term follow-up of the RTOG 9802.

PFS but not OS was improved for adult patients with LGG receiving RT + PCV versus RT alone. On post hoc analysis, for 2-year survivors, the addition of PCV to RT conferred a survival advantage, suggesting a delayed benefit for chemotherapy [2)].

Advances in molecular genetic markers, including the combined loss of chromosome arms 1p and 19q, and the mutation of the isocitrate dehydrogenase gene (IDH1/IDH2) have allowed for increased accuracy of predicting susceptibility to chemotherapeutic agents, as well as having some role in determining prognosis. PCV and temozolomide chemotherapy have both been studied when assessing progression free survival for LGG patients. Approaching patients with LGGs can be somewhat daunting given the lack of Class I evidence based protocols.

The intervening decade since the trial was completed, novel molecular markers as well as newer chemotherapy agents such as temozolomide have been developed, which make these results difficult to incorporate into clinical practice [3)].

Initial results in 2003 indicated that Temodar may be active in the treatment of low-grade glioma, and thus, further evaluation of this agent in the treatment of these tumors is warranted [4)].

1)

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