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# Congress of Neurological Surgeons systematic review and evidence-based guidelines on the management of recurrent diffuse low-grade glioma: update

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## Abstract

**Target population** These recommendations apply to adult patients with recurrent WHO grade 2 infiltrative diffuse glioma (oligodendroglioma, astrocytoma).  
**Questions and Recommendations:**  
**Imaging Q1:** In adult patients with suspected recurrence of histologically proven WHO grade 2 diffuse glioma, do advanced imaging techniques using magnetic resonance spectroscopy, perfusion weighted imaging, diffusion weighted imaging or PET provide superior assessment of tumor recurrence and histologic progression compared to standard MRI neuroimaging?  
**Recommendation Level III:** In adult patients with suspected recurrence of histologically proven WHO grade 2 diffuse glioma, advanced imaging techniques using magnetic resonance spectroscopy, perfusion weighted imaging, diffusion weighted imaging or PET are suggested for identification of tumor recurrence or histologic progression.  
**Pathology Q1:** In adult patients with suspected recurrence of histologically proven WHO grade 2 diffuse glioma, is molecular testing for IDH-1, IDH-2, and TP53 Mutations and MGMT promotor methylation mutation warranted for predicting survival and formulating treatment recommendations?  
**Recommendation Level III:** It is suggested that IDH mutation status be determined for diagnostic purposes. TP53 mutations occur early in WHO grade 2 diffuse glioma pathogenesis, remain stable, and are not suggested as a marker of predisposition to malignant transformation at recurrence or other measures of prognosis. Assessment of MGMT status is suggested as an adjunct to assessing prognosis. Assessment of CDK2NA status is suggested since this is associated with malignant progression of WHO grade 2 diffuse gliomas.  
**Q2:** In adult patients with suspected recurrence of histologically proven WHO Grade 2 diffuse glioma, is testing of proliferation indices (MIB-1 and/or BUdR) warranted for predicting survival and formulating treatment recommendations?  
**Recommendation Level III:** It is suggested that proliferative indices (MIB-1 or BUdR) be measured in WHO grade 2 diffuse glioma as higher proliferation indices are associated with increased likelihood of recurrence and shorter progression free and overall survival.  
**Chemotherapy Q1:** In adult patients with suspected recurrence of histologically proven WHO grade 2 diffuse glioma, does addition of temozolomide (TMZ), other cytotoxic agents or targeted agents to their treatment regimen improve PFS and/or OS?  
**Recommendation Level III:** Temozolomide is suggested in the therapy of recurrent WHO grade 2 diffuse glioma as it may improve clinical symptoms. PCV is suggested in the therapy of WHO grade 2 diffuse glioma at recurrence as it may improve clinical symptoms with the strongest evidence being for oligodendrogliomas. TMZ is suggested as the initial choice for recurrent WHO grade 2 diffuse glioma. Carboplatin is not suggested as there is no significant benefit from carboplatin as single agent

therapy for recurrent WHO grade 2 diffuse gliomas. There is insufficient evidence to make any recommendations regarding other agents in the management of recurrent WHO grade 2 diffuse glioma. Radiotherapy Q1: In adult patients with suspected recurrence of histologically proven WHO grade 2 diffuse glioma, does addition of radiotherapy to treatment regimen improve PFS and/or OS? Recommendation Level III: Radiation is suggested at recurrence if there was no previous radiation treatment. Q2: In adult patients with suspected recurrence of histologically proven WHO grade 2 diffuse glioma after previous radiotherapy, does addition of re-irradiation or proton therapy to the treatment regimen improve PFS and/or OS? Recommendation Level III: It is suggested that re-irradiation be considered in the setting of WHO grade 2 diffuse glioma recurrence as it may provide benefit in PFS and OS. Surgery Q1: In adult patients with suspected recurrence of histologically proven WHO grade 2 diffuse glioma, does surgical resection improve PFS and/or OS?. There is insufficient evidence to make any new specific recommendations regarding the value of surgery or extent of resection in relationship to survival for recurrent WHO grade 2 diffuse glioma.

**Keywords:** Astrocytoma; Low grade glioma; Oligodendroglioma; Recurrence.

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