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Congress of Neurological Surgeons systematic review and evidence-based guidelines for the role of chemotherapy in newly diagnosed WHO Grade II diffuse glioma in adults: update

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Abstract

Questions and recommendations from the prior version of these guidelines without changeTarget populationAdult patients (older than 18 years of age) with newly diagnosed World Health Organization (WHO) Grade II gliomas (Oligodendroglioma, astrocytoma, mixed oligoastrocytoma).QuestionIs there a role for chemotherapy as adjuvant therapy of choice in treatment of patients with newly diagnosed low-grade gliomas?RecommendationLevel III: Chemotherapy is recommended as a treatment option to postpone the use of radiotherapy, to slow tumor growth and to improve progression free survival (PFS), overall survival (OS) and clinical symptoms in adult patients with newly diagnosed LGG.QuestionWho are the patients with newly diagnosed LGG that would benefit the most from chemotherapy?RecommendationLevel III: Chemotherapy is recommended as an optional component alone or in combination with radiation as the initial adjuvant therapy for all patients who cannot undergo gross total resection (GTR) of a newly diagnosed LGG. Patients with residual tumor >1 cm on post-operative MRI, presenting diameter of 4 cm or older than 40 years of age should be considered for adjuvant therapy as well.QuestionAre there tumor markers that can predict which patients can benefit the most from initial treatment with chemotherapy?RecommendationLevel III: The addition of chemotherapy to standard RT is recommended in LGG patients that carry IDH mutation. In addition, temozolomide (TMZ) is recommended as a treatment option to slow tumor growth in patients who harbor the 1p/19q co-deletion.QuestionHow soon should the chemotherapy be started once the diagnosis of LGG is confirmed?RecommendationThere is insufficient evidence to make a definitive recommendation on the timing of starting chemotherapy after surgical/pathological diagnosis of LGG has been made. However, using the 12 weeks mark as the latest timeframe to start adjuvant chemotherapy is suggested. It is recommended that patients be enrolled in properly designed clinical trials to assess the timing of chemotherapy initiation once diagnosis is confirmed for this target population.QuestionWhat chemotherapeutic agents should be used for treatment of newly diagnosed LGG?RecommendationThere is insufficient evidence to make a recommendation of one particular regimen. Enrollment of subjects in properly designed trials comparing the efficacy of these or other agents is recommended so as to determine which of these regimens is superior.QuestionWhat is the optimal duration and dosing of chemotherapy as initial treatment for LGG?

RecommendationInsufficient evidence exists regarding the duration of any specific cytotoxic drug regimen for treatment of newly diagnosed LGG. Enrollment of subjects in properly designed clinical investigations assessing the optimal duration of this therapy is recommended.QuestionShould chemotherapy be given alone or in conjunction with RT as initial therapy for LGG? RecommendationInsufficient evidence exists to make recommendations in this regard. Hence, enrollment of patients in properly designed clinical trials assessing the difference between chemotherapy alone, RT alone or a combination of them is recommended.QuestionShould chemotherapy be given in addition to other type of adjuvant therapy to patients with newly diagnosed LGG?RecommendationLevel II: It is recommended that chemotherapy be added to the RT in patients with unfavorable LGG to improve their progression free survival.Updated Question and Recommendations from the Prior Version of These GuidelinesQuestionIn adult patients with pathologically confirmed WHO Grade II diffuse glioma does chemotherapy alone, combined with radiation therapy or after radiation therapy compared to radiotherapy alone result in better overall survival, progression free survival, local control, fewer complications, neurocognitive preservation, and quality of life?RecommendationLevel I: It is recommended that chemotherapy (PCV) be added to radiation therapy (RT) in all patients with newly diagnosed high-risk WHO Grade II diffuse glioma (Patients younger than 40 unable to get gross total resection and older than 40 regardless of the degree of resection) to improve their overall survival.

Level ii: It is recommended that chemotherapy be added to radiation therapy in all patients with newly diagnosed high-risk WHO Grade II diffuse glioma to improve overall survival without a decline in neurocognitive function.

Level iii: It is suggested that chemotherapy (temozolomide) be added to RT in all patients with newly diagnosed high-risk WHO Grade II diffuse glioma to improve progression free survival and overall survival.

Level iii: It is suggested that chemotherapy alone should be considered in patients with newly diagnosed WHO Grade II diffuse glioma in cases with 1p/19q co-deletion.New questions and recommendationsTarget populationThese recommendations apply to adult patients diagnosed with WHO Grade II diffuse glioma.QuestionIn adult patients with newly diagnosed WHO grade II diffuse glioma does administration of chemotherapy prior to surgical resection improve extent of resection, provide longer progression free survival and overall survival when compared to chemotherapy alone? RecommendationLevel III: Neo-adjuvant temozolomide may be used in patients with WHO Grade II diffuse gliomas deemed unsafe for resection due to infiltration of eloquent areas or with large contralateral extension as an initial step to improve the extent of resection.There is insufficient evidence to support a recommendation regarding the ability of chemotherapy provided prior to surgical resection to improve progression free survival (PFS) and overall survival (OS).QuestionIn adult patients with newly diagnosed WHO grade II diffuse glioma does the administration of temozolomide increase the rate of malignant transformation when compared to no chemotherapy or other chemotherapy regimens?RecommendationThere is insufficient evidence to support a recommendation against the use of temozolomide for WHO Grade II diffuse gliomas due to concern over increasing the rate of malignant transformation.QuestionIn adult patients with newly diagnosed WHO grade II diffuse glioma does administration of multi-agent chemotherapy improve progression free survival and overall survival when compared to administration of single-agent chemotherapy? RecommendationThere is insufficient evidence to support a recommendation for or against the use of multi-agent chemotherapy to improve progression free survival and overall survival when compared to administration of single-agent chemotherapy in patients with newly diagnosed WHO Grade II diffuse glioma.