clinical recommendations

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Malignant glioma: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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incidence

The incidence of malignant glioma is 5–7/100 000. Malignant glioma may develop at all ages, the peak incidence being in the fifth and sixth decades of life.

diagnosis

Malignant glioma comprises glioblastoma [World Health Organization (WHO) grade IV], anaplastic astrocytoma (WHO grade III), mixed anaplastic oligoastrocytoma (WHO grade III) and anaplastic oligodendroglioma (WHO grade III). Diagnosis after biopsy or tumor resection is made according to the revised WHO classification.

staging and risk assessment

Staging includes imaging of the brain, ideally with magnetic resonance imaging (MRI). If repeat imaging is deemed necessary to determine residual disease, it should be carried out within 24–48 h after surgery. Lumbar puncture is generally not necessary, with the exception of adult patients with medulloblastoma (in whom it should be carried out 3 weeks after surgery) and staging of other organs is not needed.

Other than lower tumor grade, good performance status and an intact neurological function, tumor resection and age <50 years have been identified as more favorable prognostic factors.

Prognosis depends on tumor grade and histology. Glioblastoma carries the worst prognosis, while pure oligodendroglioma tends to have a better outcome and improved response to therapy. Prognosis of mixed anaplastic oligoastrocytoma and anaplastic astrocytoma is intermediate between glioblastoma and pure anaplastic oligodendroglioma.

treatment plan

Patients should be evaluated by a specialized multidisciplinary team. Special consideration needs to be given to performance status and neurological function.

newly diagnosed patients

Surgery is commonly the initial therapeutic approach for debulking and obtaining tissue for diagnosis. Tumor resection is of prognostic value, and may be beneficial to attempt maximal tumor resection [II, C]. Implantation of chemotherapy-impregnated wafer (BCNU polymer) into the resection cavity has shown only a marginal benefit in malignant glioma versus radiotherapy alone [II, B].

Fractionated focal radiotherapy (60 Gy, 2 Gy × 30, or equivalent doses/fractionations) is the standard treatment after resection or biopsy [I, A]. Escalating doses beyond 60 Gy has not been shown to be of value. In elderly patients or patients with a low performance status, shorter hypofractionated regimens (e.g. 40 Gy in 15 fractions) are commonly proposed [II, B]. Radiotherapy (28 × 1.8 Gy, 50 Gy) in patients >70 years of age was superior to best supportive care alone in a randomized phase III trial [II, B].

Concomitant and adjuvant temozolomide chemotherapy has been demonstrated to significantly improve median and 2-year survival in a large randomized trial in glioblastoma [I, A]. Selecting patients likely to benefit from therapy on the basis of MGMT gene promoter methylation has been suggested [II, B].

Adjuvant chemotherapy with procarbazine, lomustine and vincristine (PCV regimen) has failed to improve survival in prospective randomized studies [I, A]. Nevertheless, based on a large meta-analysis [I, A] nitrosourea-based chemotherapy may marginally improve survival in selected patients.

recurrent disease

Some benefit of chemotherapy has been shown for patients with an adequate performance status who have not received

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prior adjuvant cytotoxic therapy. Anaplastic astrocytomas are more likely than glioblastoma to respond to chemotherapy [III, B]. For patients failing prior chemotherapy, there is no established chemotherapy regimen available and patients are best treated within investigational clinical protocols. Single-agent nitrosourea therapy may improve tumor control in some patients, while EGFR inhibition with erlotinib has not demonstrated any measurable anti-tumor efficacy in a randomized phase II trial [II, C].

Repeat surgery and implantation of chemotherapy-impregnated polymers may prolong survival in selected patients [II, B].

anaplastic oligodendroglioma

Oligodendroglioma carries a somewhat better prognosis. In particular, the subgroup of patients with a deletion on chromosome 1p and 19q seem to have a longer survival and better response to chemotherapy compared with patients without deletion. In patients with recurrent oligodendroglioma, chemotherapy should be considered [II, B], while (neo)adjuvant PCV chemotherapy [procarbazine, lomustine (CCNU), vincristine] has failed to improve survival in patients in addition to radiotherapy in newly diagnosed anaplastic oligoastrocytoma and oligodendroglioma [I, B].

response evaluation

If response is evaluated, it should be done with MRI. Contrast enhancement and presumed tumor progression on imaging 4–8 weeks after the end of radiotherapy may be an imaging artefact (pseudoprogression) and should be re-evaluated 4 weeks later with a second MRI.

Response to chemotherapy is evaluated according to the WHO criteria, but should also include an assessment of neurological function and corticosteroid use (Macdonald criteria). The rate of patients alive and progression free at 6 months (PFS_{6mo}) has been recognized as a valid endpoint and also includes patients who benefit from therapy by disease stabilization.

follow-up

Follow-up consists of a clinical evaluation with particular attention to neurological function, seizures or seizure equivalents and corticosteroid use. Patients should be tapered off steroid use as early as possible. Venous thrombotic events occur frequently in patients with unresected or recurrent tumors.

Laboratory tests are not indicated unless the patient is receiving chemotherapy (blood count), corticosteroids (glucose) or antiepileptic drugs (blood count, liver function tests).

note

Levels of evidence [I–V] and grades of recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the expert authors and the ESMO faculty.

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