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ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of malignant glioma

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 multiforme (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 MRI. If repeat imaging is deemed necessary to determine residual disease, it should be done within 24–48 h after surgery. Lumbar puncture is generally not necessary and staging of other organs is not needed.
- Other than 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. Glioblastoma carry the worst prognosis, while pure oligodendroglioma tend to have a better outcome and improved response to therapy. Mixed anaplastic oligoastrocytoma behave similarly to anaplastic astrocytoma with an intermediate prognosis.

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, but attempting maximal tumor resection remains controversial *[IV, C]*. Implantation of chemotherapy-impregnated wafer (BCNU-polymer) into the resection cavity has shown only a marginal benefit *[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 of value. In elderly patients or patients with a low performance status shorter hypofractionated regimens (e.g. 3 Gy ×10) are commonly proposed.
- Adjuvant chemotherapy with procarbazine, lomustine (CCNU) and vincristine (PCV regimen) has failed to improve survival in prospective randomized studies *[I, A]*. Nevertheless, based on a large meta-analysis *[III, B]* nitrosourea-based chemotherapy may improve survival in selected patients.
- Concomitant and adjuvant temozolomide chemotherapy has demonstrated to significantly improve median and 2-year survival in a large randomized trial *[I, A]*. Selecting patients likely to benefit from therapy based on *MGMT* gene methylation has been suggested *[II, B]*.

Recurrent disease

- Some benefit of chemotherapy has been shown for patients with an adequate performance status who have not received prior adjuvant cytotoxic therapy. Anaplastic astrocytomas are more likely to respond to chemotherapy than glioblastoma. *[III, B]*.
- Repeat surgery and implantation of chemotherapy-impregnated polymers may prolong survival in selected patients *[II, B]*.

Oligodendroglioma

- Oligodendroglioma carry 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. However, at the current time 1p/19q LOH determination should not be routinely performed and should not influence the initial treatment recommendations. In patients with recurrent oligodendroglioma, chemotherapy should be considered *[II, 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 artifact due to changes in the blood-brain barrier permeability and should be confirmed 4 weeks later with a second MRI.
- Response to chemotherapy is evaluated according to the WHO criteria, but should also include an assessment of the neurological function and corticosteroid use (Macdonald criteria).

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.
- Laboratory tests are not indicated unless patient is receiving chemotherapy (blood counts), corticosteroids (glucose) or anti-epileptic drugs (blood counts, 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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