25th World Congress of Neurology

Teaching Couse Neuro-Oncology

WFN / SOCIETY OF NEURO-ONCOLOGY JOINT SESSION

Standards of Care in Neuro-Oncology: Gliomas

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Conflicts of interest

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Learning objectives

- Understand the concepts underlying the new 2021 WHO classification of gliomas

- Understand the contributions of surgery, radiotherapy and pharmacotherapy to outcome in various types of gliomas

- Understand the current controversies in the diagnosis and management of gliomas

Key messages

- **Diffuse gliomas of adulthood are defined based on histomorphological and on molecular genetic features in the 2021 WHO classification**
- **Combined modality treatment of surgery followed by chemoradiotherapy improves outcome in all glioma subtypes, but is not curative**
- **Novel approaches of targeted therapy and immunotherapy may provide benefit in subgroups of glioma patients**
- **Standardized multidisciplinary approaches to glioma-associated complications, e.g., epilepsy and vascular complications, are an important aspect of a comprehensive approach to glioma patients**

EANO 2021 - Recommendations

General	C	L
Karnofsky performance score (KPS), neurological function, age, and individual risks and benefits should be considered for clinical decision making.	IV	-
Screening and prevention have no major role for patients with gliomas.	IV	-
Patients with relevant germ line variants or suspected hereditary cancer syndromes should receive genetic counselling and based on that might be referred for molecular genetic testing.	IV	-
The diagnostic imaging modality of first choice is magnetic resonance imaging (MRI) without and with gadolinium-based contrast agent administration.	IV	-
Pseudoprogression should be considered in patients with an increase of abnormalities on neuroimaging in the first months after local therapeutic interventions including radiotherapy and experimental local treatments.	II	B
Clinical decision making without obtaining a definitive WHO diagnosis at least by biopsy should occur only in very exceptional situations.	IV	-

EANO 2021 - Recommendations

Pathology	C	L
Glioma classification should follow the most recent WHO classification of tumors of the central nervous system, complemented by cIMPACT-NOW updates.	IV	-
Immunohistochemistry for mutant IDH1-R132H protein and nuclear expression of ATRX should be performed routinely in the diagnostic assessment of gliomas.	IV	-
If immunohistochemistry for IDH1-R132H is negative, sequencing of IDH1 codon 132 and IDH2 codon 172 in all WHO grade 2 and 3 astrocytic and oligodendroglial gliomas and in all glioblastomas of patients younger than 55 years of age should be done to allow for integrated diagnoses according to the WHO classification and to guide treatment decisions.	IV	-
1p19q codeletion status should be determined in all IDH-mutant gliomas with retained nuclear expression of ATRX.	I	B
MGMT promoter methylation status should be determined in elderly patients with glioblastoma and in IDH-wildtype WHO grade II/III gliomas to guide decision for the use of temozolomide instead of or in addition to radiotherapy.	I	B
CDKN2A homozygous deletions should be explored in IDH-mutant diffuse astrocytomas.	IV	B
Chromosome 7 gain with chromosome 10 loss (+7/-10), EGFR amplification, and TERT promoter mutation should be tested in IDH wildtype diffuse gliomas lacking microvascular proliferation and necrosis as histological features of WHO grade 4 to allow for a diagnosis of glioblastoma, IDH-wildtype.	IV	-
Assessment of H3-K27M status should be done in diffuse gliomas involving the midline.	IV	-
BRAF-V600 mutations may be explored in IDH-wildtype diffuse gliomas.	IV	-

EANO 2021 - Recommendations

Surgery	C	L
Since extent of resection is a prognostic factor, efforts at obtaining complete resections are justified across all glioma entities.	IV	-
The prevention of new permanent neurological deficits has higher priority than extent of resection in the current surgical approach to gliomas.	IV	-

EANO 2021 - Recommendations

IDH-mutant WHO grade 2, 3 and 4 gliomas	C	L
Standard of care for (1p/19q-non-codeleted) WHO grade 2 diffuse astrocytoma requiring further treatment includes resection as feasible or biopsy followed by involved field radiotherapy and maintenance PCV polychemotherapy (RTOG 9802).	II	B
Standard of care for 1p/19q-non-codeleted anaplastic astrocytoma includes resection as feasible or biopsy followed by involved field radiotherapy and maintenance temozolomide (CATNON).	II	B
Patients with 1p/19q-codeleted WHO grade 2 oligodendroglial tumors requiring further treatment should be treated with radiotherapy followed by PCV polychemotherapy.	III	B
Patients with 1p/19q-codeleted anaplastic oligodendroglial tumors should be treated with radiotherapy followed by PCV polychemotherapy (EORTC 26951, RTOG 9402).	II	B
Temozolomide chemotherapy is standard treatment at progression after surgery and radiotherapy for most patients with WHO grade 2 and 3 gliomas.	II	B

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EANO 2021 - Recommendations

Glioblastoma, IDH-wildtype (WHO grade 4)	C	L
Standard of care for glioblastoma, IDH-wildtype (age < 70 years, KPS ≥ 70) includes resection as feasible or biopsy followed by involved-field radiotherapy and concomitant and maintenance (6 cycles) temozolomide chemotherapy (EORTC 26981 NCIC CE.3).	I	A
Temozolomide is particularly active in patients with MGMT promoter-methylated tumors whereas its activity in patients with MGMT promoter-unmethylated tumors is marginal.	II	B
Elderly patients not considered candidates for temozolomide chemoradiotherapy should be treated based on MGMT promoter methylation status (NOA-08, Nordic Trial) with radiotherapy (e.g., 15 x 2.66 Gy) or temozolomide (5/28) alone.	II	B
At recurrence, standards of care are less well defined. Nitrosourea regimens, temozolomide re-challenge and, with consideration of the country-specific label, bevacizumab are options of pharmacotherapy, but an impact on overall survival remains unproven. When available, recruitment into appropriate clinical trials should be considered.	II	B

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