Glioma treatment

Low-Grade Gliomas (Grade 2)

- **IDH-mutant, 1p/19q-codeleted (oligodendroglioma)**:
  - Maximal safe resection.
  - Observation vs. RT + PCV chemotherapy if high-risk (age >40, subtotal resection).
- **IDH-mutant, non-codeleted (astrocytoma)**:
  - Surgery.
  - Adjuvant RT + TMZ if high-risk.

High-Grade Gliomas (Grade 3-4)

- **Grade 3 Astrocytoma (IDH-mutant)**:
  - Maximal resection.
  - RT + adjuvant TMZ.
- **Glioblastoma (IDH-wildtype, Grade 4)**:
  - Maximal safe resection.
  - Radiotherapy (60 Gy in 30 fractions) + concomitant TMZ.
  - 6+ cycles of adjuvant TMZ.

3. Targeted and Experimental Therapies

- Tumor-Treating Fields (TTF): Approved for glioblastoma.
- Bevacizumab: Recurrent GBM (symptom control).
- Clinical trials: immunotherapy, vaccines, CAR-T, IDH inhibitors (e.g., vorasidenib), oncolytic viruses.

4. Supportive Care

- **Anticonvulsants**: Levetiracetam preferred.
- **Corticosteroids**: Dexamethasone for edema.
- **Neuropsychology**: Cognitive rehab, support.
- **Palliative care**: Early integration in high-grade cases.

5. Follow-Up

- MRI every 3–6 months initially.
- Use RANO criteria for progression.
- Monitor for pseudoprogression (especially <3 months post-RT).

6. Recurrent Disease

- Surgical re-resection (if feasible).
- Re-irradiation in selected patients.
- Systemic therapy: Bevacizumab, lomustine, trials.
- Best supportive care in poor prognosis cases.

Significant effort has been made to investigate immunotherapy and precision oncology approaches. While there are many promising treatment strategies, none fundamentally changed the management of glioma patients. However, we are still awaiting the outcome of ongoing trials, which have the potential to revolutionize the treatment of glioma [1)].

Window of opportunity clinical trial designs can provide early insight into the biological plausibility of a novel therapeutic strategy in the clinical setting. A variety of window-of-opportunity trial designs, which take into account the limited access to treated tissue and the challenges with obtaining pretreatment control tissues, have been used for the initial development of traditional and targeted small-molecule drugs and biologic therapies, including immunotherapies and oncolytic viral therapies. Early-stage development of glioma treatment should include a window-of-opportunity component whenever feasible [2)].

4-methylumbelliferone (4-MU), a small competitive inhibitor of Uridine diphosphate (UDP) with the ability to penetrate the blood-brain barrier (BBB), inhibited glioma cell proliferation in vitro and in vivo. Thus, approaches that interfere with Hyaluronic acid metabolism by altering the expression of HAS3 and CD44 and the administration of 4-MU potentially represent effective strategies for glioma treatment [3)].

Recent advances in translational research and molecular understanding of brain tumors raise hope that new treatments are imminent, and patients should be encouraged to participate in clinical trials. The general practitioners (GPs) has an important role in patient support and coordination of care [4)].

Molecularly-targeted therapy is a focus of glioma research.

Current standard treatment for glioma patients is surgical removal followed by radiotherapy and adjuvant chemotherapy. Due to therapeutic resistance and tumor recurrence, efforts are ongoing to identify the molecules that are fundamental to regulate the tumor progression and provide additional methods for individual treatment of glioma patients. By studying the initiation and maintenance of glioma, studies focused on the targets of tyrosine kinase receptors including EGFR, PDGFR and other crucial signal pathways such as PI3K/AKT and RAS/RAF/MAPK pathway. Furthermore, recent advances in targeting immunotherapy and stem cell therapy also brought numerous strategies to glioma treatment [5)].

Evidence have shown that a recombinant adenoviral vector expressing human wild-type p53, granulocyte-macrophage colony-stimulating factor (GM-CSF), and B7-1 genes (BB-102) may have antitumor effects in vitro. In this study, we investigated the effects of BB-102-based vaccine on glioma in vivo. An animal model using nonobese diabetic/severe combined immunodeficiency (NOD/SCID) mice with human immune system was established. The mice were vaccinated with inactivated U251 glioma cells transduced with BB-102 or adenoviral vector expressing green fluorescence protein (Ad-GFP) as a control and followed by the challenge of live U251 glioma cells. Tumor growth and antitumor responses were measured. Data showed that mice vaccinated with BB-102 had significantly reduced local tumor growth compared to mice with Ad-GFP vaccination or the control group. Histopathological analysis displayed low tumor cell density and significant infiltration of human peripheral blood lymphocytes (HuPBLs) in the tumor tissues of mice transduced with BB-102. Immunohistochemical analysis showed that mutant p53 was not expressed in tumor tissues of mice with BB-102 vaccination, and the expression level of Ki67 was significantly lower in the tumor tissues of the BB-102 group than those in the Ad-GFP group or the control group. Further study demonstrated that mice with BB-102 vaccination had significantly increased total T cell numbers, total T cell proportion, CD4+ T cell proportion, and CD8+ T cell proportion in spleens, as well as higher value of IgG, IgA, and IgE in sera. These data suggest that the recombinant adenoviral vector expressing human wild-type p53, GM-CSF, and B7-1 genes could suppress glioma in NOD/SCID mice model and might be considered as a novel strategy for glioma therapy [6].

Treatment options depend on the type of glioma, and patient-specific factors such as location and size of the glioma, patient age, symptoms and neurological status. In addition, three molecular markers – 1p/19q co-deletion, O6-methylguanine methyltransferase (MGMT) promoter methylation and isocitrate dehydrogenase (IDH) 1/2 mutations – are known to have important diagnostic, prognostic and predictive (for treatment efficacy) roles in glioma treatment (for reviews see Tabatabai et al. 2010 [7] and Leu et al. [8].

The therapeutic management and prognosis of cerebral gliomas depend on tumor type and grade, and on exact definition of boundary [9] [10] [11].

In glioma patients, a presumed eloquent location has been identified as a key variable influencing the treatment strategy [12] [13].

Surgery

see Glioma surgery

High-grade glioma treatment

see High-grade glioma treatment.

Glioma immunotherapy

Glioma immunotherapy.

Glioma Radiosurgery

Glioma Radiosurgery.

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