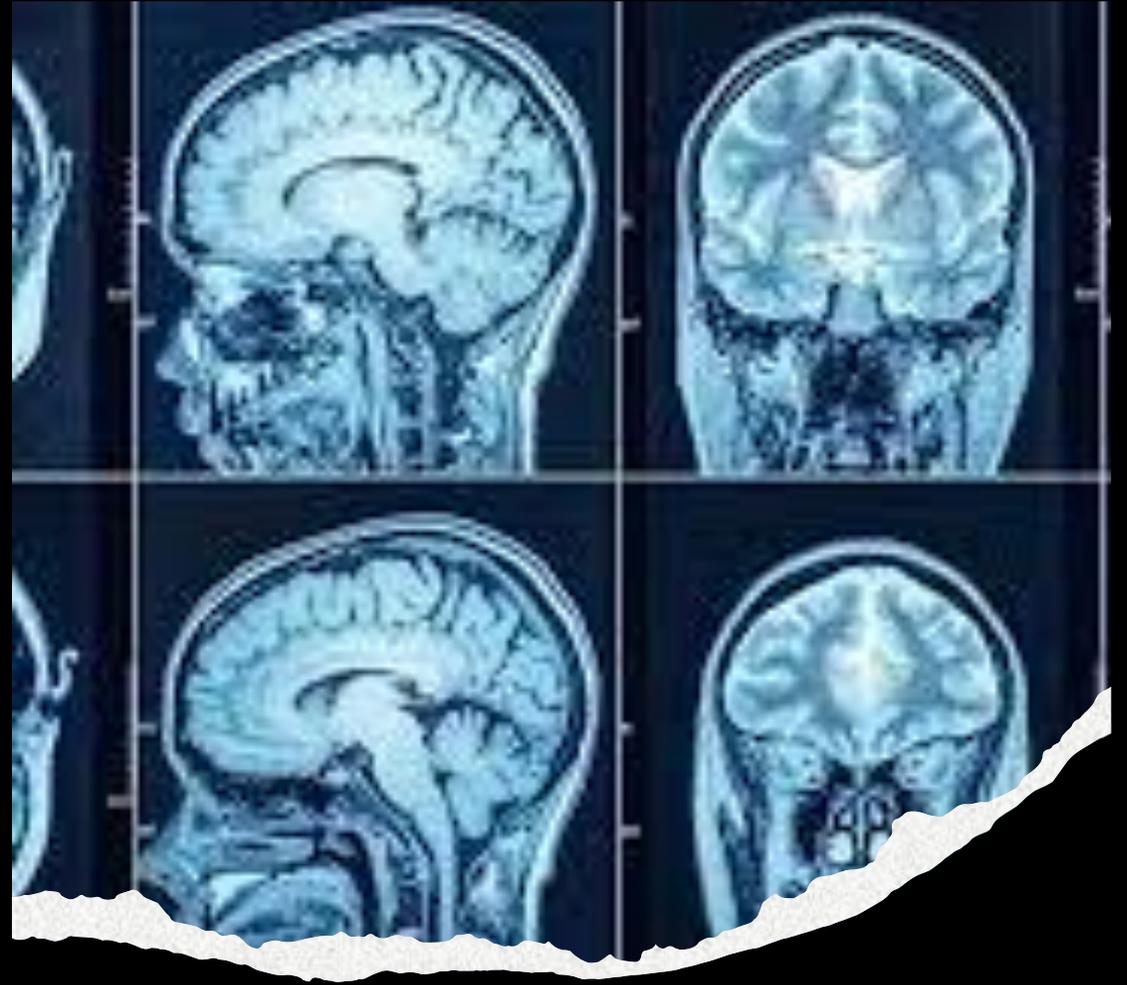


Glioblastoma: A Therapeutic Challenge

Sanya Badole
BIOS 4500 / BIOL 8803: Drug Discovery

Selected Disease Presentation
Date: February 2, 2026



What is Glioblastoma?

- Most aggressive primary malignant brain tumor, classified as WHO Grade IV diffuse glioma
- Arises from glial cells in the central nervous system
- Historically termed "glioblastoma multiforme" (GBM); WHO 2021 classification discontinued this term
- Modern diagnosis: Glioblastoma, IDH-wildtype (integrated histologic and molecular classification)

Clinical Symptoms

- Neurological Manifestations:

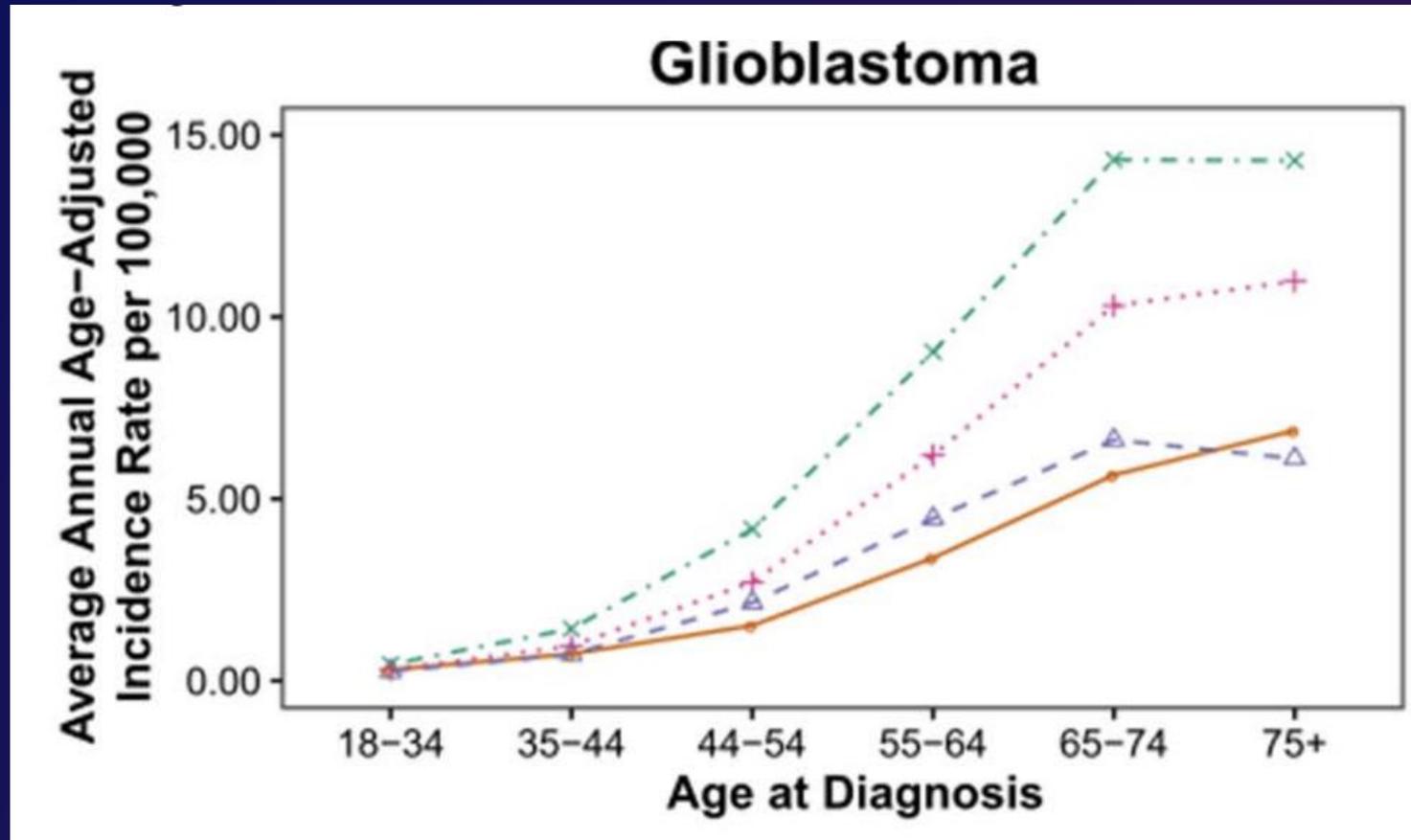
- Progressive headaches (worse in morning)
- Seizures (even in patients with no prior history)
- Cognitive decline and memory loss
- Personality changes and confusion

- Functional Impairments:

- Vision changes (blurred/double vision)
- Speech difficulties
- Motor weakness (face, arms, legs)
- Loss of coordination and balance

Affected Population - Demographics

- Age Distribution:
 - Median age at diagnosis: 64 years
 - Highest incidence in patients ≥ 65 years (6.24 per 100,000)
 - Annual incidence increases with age (0.5 per 100,000 in ages 20-35 to 15 per 100,000 in ages 75-85)
- Gender & Ethnicity:
 - Male-to-female ratio: 1.6:1 (60% higher in males)
 - Highest incidence in non-Hispanic whites (4.71 per 100,000)
 - Lower incidence in African Americans and Asian/Pacific Islanders

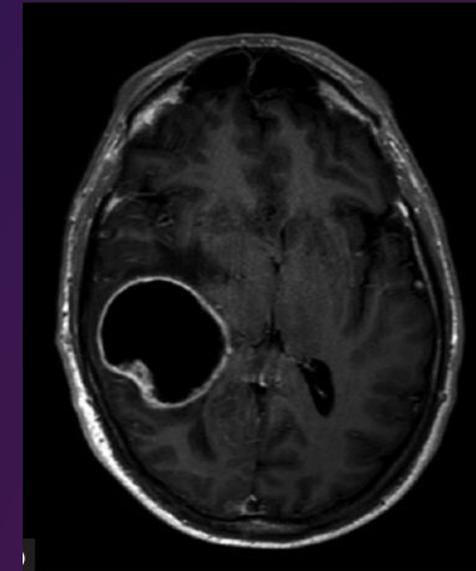
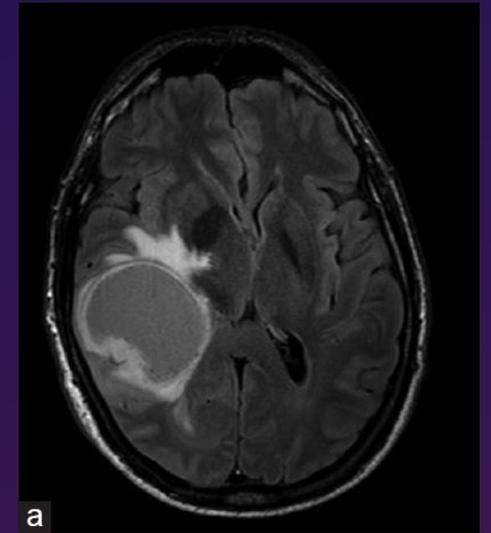


—○— Asian or Pacific Islander
 -△- Black
 ·+· Hispanic White
 ·x· Non-Hispanic White

Figure Reference : Ostrom, Quinn T et al. "Adult Glioma Incidence and Survival by Race or Ethnicity in the United States From 2000 to 2014." *JAMA oncology* vol. 4,9 (2018): 1254-1262. doi:10.1001/jamaoncol.2018.1789

Diagnosis

- Clinical Presentation & Exam
 - Neurological exam reveals focal deficits (motor, language, vision) or cognitive changes
- Neuroimaging
 - MRI brain with gadolinium: ring-enhancing mass with central necrosis and surrounding edema
 - Advanced imaging (perfusion, spectroscopy, FET-PET) helps grade and distinguish from mimics
- Tissue Diagnosis (Gold Standard)
 - Stereotactic biopsy or surgical resection for histopathology
 - Microscopic features: malignant astrocytes, high mitotic activity, microvascular proliferation, necrosis
- Molecular Testing
 - IDH1/2 mutation, MGMT methylation, 1p/19q codeletion, TERT promoter status
 - Required for WHO classification and guides prognosis and treatment decisions



Prognosis & Disease Burden

- Survival Statistics:
 - Median survival: 15 months post-diagnosis
 - 5-year survival rate: <10%
 - Highly aggressive with rapid progression
- Clinical Challenges:
 - Fast tumor growth
 - High recurrence rate
 - Infiltrative nature makes complete resection difficult
 - Blood-brain barrier limits drug delivery

Current Treatment Options

- Standard of Care (Stupp Protocol):
 - Surgical resection: Maximal safe resection
 - Radiation therapy: 60 Gy over 6 weeks
 - Chemotherapy: Temozolomide (concurrent and adjuvant)
- Limitations:
 - Tumor recurrence in nearly all cases
 - Treatment resistance
 - Significant side effects

Emerging Therapies

- Advanced Approaches (2026):
 - Tumor Treating Fields (TTFields/Optune)
 - Bevacizumab (anti-angiogenic therapy)
 - Targeted molecular therapies (IDH mutations, MGMT methylation status)
- Investigational Therapies:
 - Immunotherapy (checkpoint inhibitors, CAR-T cells)
 - Dendritic cell vaccines
 - Oncolytic viral therapy
 - Gene therapy trials (starting early 2026)

Unmet Medical Need & Rationale for Drug Discovery

- Why Glioblastoma?

- Poor prognosis despite aggressive treatment
- Limited treatment options beyond standard of care
- High rate of recurrence and resistance
- Significant impact on quality of life
- Critical need for novel therapeutic approaches

- Drug Discovery Opportunity:

- Multiple targetable pathways
- Growing understanding of tumor heterogeneity
- Potential for precision medicine approaches

Thank You!

References

1. Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. *Neuro Oncol*. 2021;23(8):1231-1251. doi:10.1093/neuonc/noab106
2. Ostrom QT, Cioffi G, Gittleman H, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2016-2020. *Neuro Oncol*. 2023;25(Suppl 4):iv1-iv99. doi:10.1093/neuonc/noad149
3. Ostrom QT, Price M, Ryan K, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2017-2021. *Neuro Oncol*. 2024;26(Suppl 6):vi1-vi87. doi:10.1093/neuonc/noae165
4. American Brain Tumor Association. Glioblastoma (GBM). 2025. Available at: https://www.abta.org/tumor_types/glioblastoma-gbm/
5. Weller M, Wick W, Aldape K, et al. Glioma. *Nat Rev Dis Primers*. 2015;1:15017. doi:10.1038/nrdp.2015.17
6. Ostrom QT, Cote DJ, Ascha M, et al. Adult Glioma Incidence and Survival by Race or Ethnicity in the United States From 2000 to 2014. *JAMA Oncol*. 2018;4(9):1254-1262. doi:10.1001/jamaoncol.2018.1789
6. Shen Y, Wasilewski M, Moser RP, et al. Impact of Age and Gender on Survival of Glioblastoma Multiforme Patients: A Multicenter Retrospective Study. *Front Surg*. 2024;11:1541054. doi:10.3389/fsurg.2024.1541054
7. Yang W, Warrington NM, Taylor SJ, et al. Sex Differences in GBM Revealed by Analysis of Patient Imaging, Transcriptome, and Survival Data. *Sci Transl Med*. 2019;11(473):eaa05253. doi:10.1126/scitranslmed.aao5253
8. Thakkar JP, Dolecek TA, Horbinski C, et al. Age at diagnosis and sex interact to modify primary malignant glioma incidence and survival. *Neuro Oncol*. 2022;24(2):311-319. doi:10.1093/neuonc/noab166
9. Schaff LR, Mellinghoff IK. Glioblastoma and Other Primary Brain Malignancies in Adults: A Review. *JAMA*. 2023;329(7):574-587. doi:10.1001/jama.2023.0023
11. Mayo Clinic. Glioblastoma - Symptoms and Causes. Updated December 2024. Available at: <https://www.mayoclinic.org/diseases-conditions/glioblastoma/symptoms-causes/syc-20569077>
12. Weill Cornell Medicine. Symptoms of Glioblastoma Multiforme. Available at: <https://neurosurgery.weillcornell.org/condition/glioblastoma-multi-forme-gbm>
13. National Organization for Rare Disorders (NORD). Glioblastoma Multiforme. Updated 2023. Available at: <https://rarediseases.org/rare-diseases/glioblastoma-multi-forme/>
14. Liang S, Fan X, Zhao M, et al. Subtle neuropsychiatric symptoms of glioblastoma multiforme: a systematic review. *J Clin Neurosci*. 2020;73:274-279. doi:10.1016/j.jocn.2020.01.079
15. Goebel S, Mehdorn HM. Depression and anxiety in glioma patients: a narrative review. *Neurooncol Pract*. 2023;10(4):335-345. doi:10.1093/nop/npad018
16. Rooney AG, Carson A, Grant R. Depression in cerebral glioma patients: a systematic review of observational studies. *J Natl Cancer Inst*. 2011;103(1):61-76. doi:10.1093/jnci/djq458
17. Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med*. 2005;352(10):987-996. doi:10.1056/NEJMoa043330

References

17. Stupp R, Hegi ME, Mason WP, et al. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. *Lancet Oncol.* 2009;10(5):459-466. doi:10.1016/S1470-2045(09)70025-7
18. Weller M, van den Bent M, Preusser M, et al. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. *Nat Rev Clin Oncol.* 2021;18(3):170-186. doi:10.1038/s41571-020-00447-z
20. Tykocki T, Eltayeb M. Ten-year survival in glioblastoma: a systematic review. *J Clin Neurosci.* 2018;54:7-13. doi:10.1016/j.jocn.2018.05.002
21. Tamimi AF, Juweid M. Epidemiology and Outcome of Glioblastoma. In: De Vleeschouwer S, ed. *Glioblastoma*. Codon Publications; 2017. Chapter 8. doi:10.15586/codon.glioblastoma.2017.ch8
22. Rasmussen BK, Hansen S, Laursen RJ, et al. Epidemiology of glioma: clinical characteristics, symptoms, and predictors of glioma patients grade I-IV in the Danish Neuro-Oncology Registry. *J Neurooncol.* 2017;135(3):571-579. doi:10.1007/s11060-017-2607-5
23. Arvanitis CD, Ferraro GB, Jain RK. The blood-brain barrier and blood-tumour barrier in brain tumours and metastases. *Nat Rev Cancer.* 2020;20(1):26-41. doi:10.1038/s41568-019-0205-x
24. van Tellingen O, Yetkin-Arik B, de Gooijer MC, et al. Overcoming the blood-brain tumor barrier for effective glioblastoma treatment. *Drug Resist Updat.* 2015;19:1-12. doi:10.1016/j.drug.2015.02.002
Cancer Genome Atlas Research Network. Comprehensive genomic characterization defines human glioblastoma genes and core pathways. *Nature.* 2008;455(7216):1061-1068. doi:10.1038/nature07385
25. Brennan CW, Verhaak RG, McKenna A, et al. The somatic genomic landscape of glioblastoma. *Cell.* 2013;155(2):462-477. doi:10.1016/j.cell.2013.09.034

