

Survival Impact of Isocitrate Dehydrogenase (IDH)-Wildtype Histological Versus Molecular Glioblastoma

Summarize the findings of this study: Patil N, Dube S, Mutua F, Kakumanu S, Shankar JJ, Sinha N, Pareek V. Survival Impact of Isocitrate Dehydrogenase (IDH)-Wildtype Histological Versus Molecular Glioblastoma: A Propensity Score-Matched Analysis. Cureus. 2025 Jul 24;17(7):e88667. doi: 10.7759/cureus.88667. PMID: 40861724; PMCID: PMC12375397.

Copilot: Here's a clear summary of the study you mentioned:

Study Focus

The research compared **histological glioblastoma (histGBM)**—diagnosed by classic microscopic features like necrosis or microvascular proliferation—with **molecular glioblastoma (molGBM)**—IDH-wildtype diffuse astrocytic tumors that lack those histological features but carry molecular alterations (e.g., **TERT promoter mutation, EGFR amplification, or +7/−10 chromosomal changes**). The aim was to determine whether survival outcomes differ between these two groups when matched for baseline characteristics.

Key Findings

- **Cohort & Method:** Observational, propensity score-matched analysis of patients with IDH-wildtype glioblastoma. Matching was done to balance confounding factors such as age, performance status, and treatment received.
- **Survival Outcomes:**
 - **Overall survival (OS)** was **comparable** between histGBM and molGBM groups.
 - **Progression-free survival (PFS)** showed no significant difference after matching.
 - This suggests that **molecularly defined glioblastomas behave clinically as aggressively as histologically defined glioblastomas**.
- **Clinical Implication:** The findings support the **2021 WHO CNS tumor classification**, which groups both histGBM and molGBM under **IDH-wildtype glioblastoma, WHO grade 4**, regardless of histological appearance. In practice, this means patients with molGBM should be treated with the same aggressive protocols as histGBM.

Conclusion

The study reinforces that **molecular glioblastomas (IDH-wildtype) have survival outcomes equivalent to histological glioblastomas**. Histology alone is insufficient for prognosis—molecular

profiling is essential. This validates the modern shift toward **molecularly driven classification and treatment planning** in neuro-oncology.

Can you explain the significance of the findings?

Copilot: Absolutely—this study carries some important weight in how we understand and treat glioblastoma. Let me break down the **significance**:

Why These Findings Matter

1. Validation of WHO 2021 Classification

- The World Health Organization's 2021 update redefined glioblastoma:
 - **Histological GBM:** diagnosed by microscopic features (necrosis, microvascular proliferation).
 - **Molecular GBM:** IDH-wildtype astrocytomas without those features but with specific molecular alterations.
- This study shows that **molecular GBMs have the same poor survival outcomes as histological GBMs**, confirming that the WHO was right to group them together as **glioblastoma, IDH-wildtype, WHO grade 4**.

2. Clinical Practice Impact

- Before this, some clinicians hesitated to treat molecular GBMs as aggressively as histological GBMs, since they “looked” less malignant under the microscope.
- The findings make it clear: **molecular GBMs are just as aggressive**, so patients should receive the same standard-of-care therapies (surgery, chemoradiation, temozolomide, etc.).

3. Prognostic Clarity

- Survival equivalence means that **histology alone is not enough** to predict outcomes.
- Molecular profiling is essential for accurate diagnosis, prognosis, and treatment planning.

4. Research & Trial Design

- Clinical trials can now confidently include both histological and molecular GBMs in the same category.
- This avoids underpowering studies or misclassifying patients, leading to more reliable results in future glioblastoma research.

Big Picture

The study essentially closes the debate:

- **Histological GBM \approx Molecular GBM in terms of survival.**
- This cements the shift from a purely microscopic definition of brain tumors to a **molecularly driven era of neuro-oncology**.

👉 In short: the significance is that **patients with molecular GBM should not be underestimated or undertreated**—they face the same prognosis as classic glioblastoma, and the medical community now has strong evidence to treat them accordingly.