Assessment of Age in the Clinical Risk Stratification of Patients with IDH-Mutant Gliomas

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Background

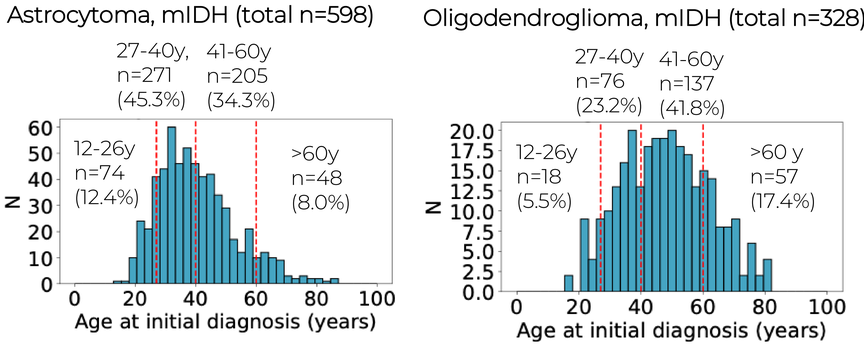
- Prognosis for patients with mutant isocitrate dehydrogenase (mIDH) gliomas is influenced by tumor type, size, neurologic deficits, and age.
- Traditionally, patients > 45 years old are considered high-risk, prompting consideration of early chemoradiation.
- Recent promising results with the mIDH inhibitor vorasidenib challenge traditional age-based risk stratification, sparking debate over its role in treatment decisions.
- We evaluated survival relative to age and molecular data obtained from next-generation sequencing (NGS).

Methods

- Brain tumor specimens from patients with IDH mutant glioma were analyzed using NGS and WTS at Caris Life Sciences (Phoenix, AZ).
- Samples were stratified by age at diagnosis into four groups:
  - 12-26 years of age
  - 27-40 years of age
  - 41-60 years of age
  - >60 years of age
- Real-world overall survival (calculated from initial diagnosis to last contact) was obtained from insurance claims data and analyzed using Kaplan-Meier and Cox proportional hazards models.
- Covariates in the multivariate regression analysis included radiation therapy treatment, temozolomide treatment, and mutation status of different key genetic/molecular biomarkers.
- For each subtype, comparisons in survival were made between patients 27-40y vs. 41-60y given larger sample size, and patients with temozolomide treatment before biopsy were excluded (about 10%).

Results

Figure 1: Age Distribution in Our Cohort of Patients with mIDH Glioma



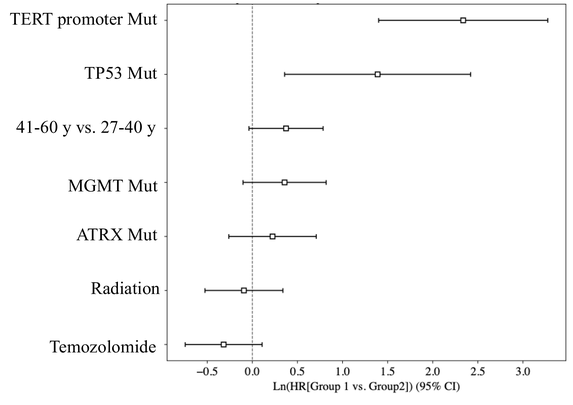


Figure 2: Hazard Ratio Comparing mIDH Astrocytoma Patients Ages 41-60 years vs. 27-40 years

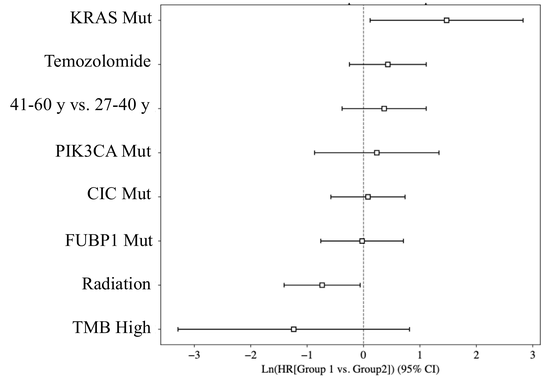


Figure 3: Hazard Ratio Comparing mIDH Oligodendroglioma Patients ages 41-60 years vs. 27-40 years

Conclusions

- In this enriched dataset of patients with mIDH low grade glioma, which included critical data from NGS, age did not contribute to survival differences when comparing patients between 27-40 years with those aged 41-60 years.
- Rather, selected genetic alterations , such as KRAS for patients with oligodendroglioma and TP53 and TERT mutations for patients with astrocytoma, were associated with poorer survival.
- The results suggest that data gleaned from NGS, rather than age, may drive prognosis for mIDH glioma patients.

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