

Sex differences in GBM treatment response: an observational study

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Background

Glioblastoma (GBM) is the most common malignant primary brain tumor in adults and is linked to poor survival due to its invasive and aggressive nature. Males and females differ in tumor behavior across many cancers [1], and in GBM there are notable sex differences in incidence rates. Analysis from a preliminary data set coming from image-localized biopsies demonstrated females had significantly less tumor cell density in the non-enhancing portion of the tumor vs males.

Sex Differences in Tumor Invasion





These findings led us to hypothesize that males and females may receive different levels of benefit from extensive surgical resections. We further hypothesized that the cells were ultimately behaving differently and thus may demonstrate a sex-specific response to temozolomide.

Methods

Drawing from our extensive multi-institutional brain tumor repository, we investigated GBM subjects with overall survival (OS), extent of resection (EOR), number of temozolomide (TMZ) cycles, and sex data. Cox proportional hazard ratios were computed to investigate the multivariable predictive value of the patient variables with OS. Patients were then divided into groups based on their sex, EOR (either biopsy/subtotal resection (STR) or gross total resection), and TMZ cycles (I: <6 cycles, II: 7-11 cycles and III: >12 cycles).

| Cohort Summary | Males N=387 | Females N=233 |
|--------------------|----------------|------------------|
| Median Age (years) | 57 | 58 |
| Median OS (days) | 706 | 751 |
| TMZ Group I | N=157 | N=93 |
| TMZ Group II | N=27 | N=20 |
| TMZ Group III | N=32 | N=14 |
| EOR - GTR | N=110 | N=66 |
| EOR - STR | N=116 | N=61 |
| EOR - Biopsy | N=53 | N=36 |



Females may benefit from less extensive surgical resection



Females may benefit from fewer TMZ cycles



Results

Multivariate Predictors of Overall Survival

Discussion **Overall Survival** Males (N = 129) 100 Survival of Females (N = 87) p-value: 0.0391 % 1000 2000 3000 4000 5000 Days elapsed

Acknowledging sex differences in GBM patients and moving towards precision medicine, it is critical to further investigate treatment responses between the sexes to identify the differences and eventually apply the best possible treatment to each sex.

Future Work

- Validate results in larger cohorts
- Quantitatively assess EOR status utilizing pre – and post-surgical MR imaging
- Assess sex differences and investigate underlying mechanisms utilizing new data from an ongoing clinical trial involving image-localized biopsies from distinct regions of the tumor

References

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Graphic created with BioRender.com

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