Extent of Resection and MGMT Promotor Methylation Status are Independent Risk Factors in IDH1_R132H Wild-type Primary Glioblastomas

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Introduction

Tumor resection has long played a role in the treatment of brain tumors. Previous pivotal studies on the influence of extent of resection (EOR) in primary glioblastoma (GBM) have failed to incorporate molecular tumor markers that were introduced in the 2016 update of the WHO classification of brain tumors.

Thus, the impact of extensive surgical approaches in the light of MGMT methylation and/or IDH mutation status is unclear.

Methods

We retrospectively analyzed our prospectively collected database of patients undergoing surgery for newly diagnosed GBM WHO °IV and included only IDH1_R132H wild-type patients.

All patients had volumetric assessment of EOR and received adjuvant treatment according to local tumor board recommendation and patient preference.

We hypothesized that gross total resection was associated with better outcome. This analysis was approved by our local ethics committee.

Results

175 patients (median age: 60 years) were included in this analysis.

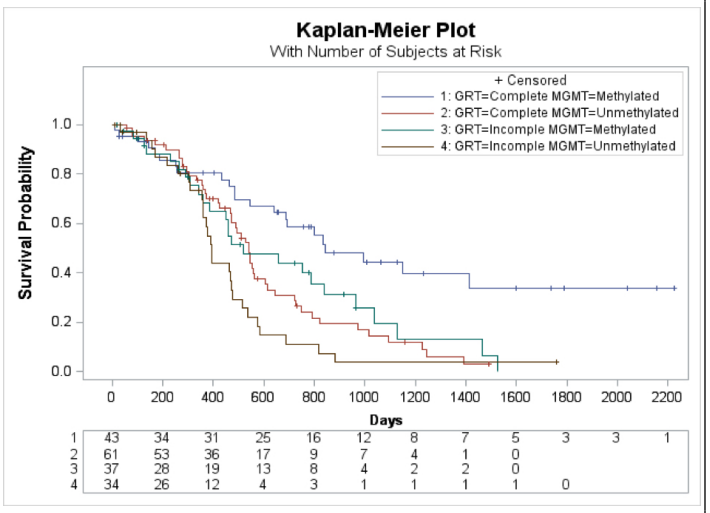
Median overall survival (OS) was 18.0 months. MGMT promotor methylation was present in 80 patients (45.7%). Complete removal of contrast-enhancing tissue (CRET) was achieved in 104 patients (59.4%).

In Cox regression analysis, both MGMT-promoter methylation (HR 1.55; 95% CI, 1.01-2.19; p=0.013) and CRET (HR 1.48; 95% CI, 1.06-2.07; p=0.020) were significantly associated with favorable progression-free survival (PFS). Further, both MGMT promotor methylation (HR 2.13; 95% CI, 1.45-3.12; p=0.0001) and CRET (HR 1.81; 95% CI, 1.24-2.63; p=0.002) were independently associated with longer OS. No benefit was seen for resections of less than 99% of the tumor volume.

Of other risk factors analyzed, only age (>60 vs. <=60 years) was significantly associated with PFS (HR 1.60; 95% CI, 1.14-2.24; p=0.006) and OS (HR 2.19; 95% CI, 1.51-3.19; p<0.0001).

We observed that CRET may overcome the biological disadvantage of an unmethylated MGMT promotor: no significant outcome differences were observed between non-MGMT methylated patients undergoing CRET, and non-CRET, MGMT methylated patients (PFS: p=0.726; OS: p=0.477).

Overall survival



Kaplan Meier curve showing overall survival stratified by MGMT promotor methylation status and extent of tumor resection

Conclusions

Both CRET and MGMT promotor methylation are independent prognostic factors for improved OS and PFS. Our study incorporates molecular markers and our data highlight the importance of aggressive surgical approaches. If achieved, CRET might compensate for the biological disadvantage of lacking MGMT promotor methylation.