Glioblastoma Recurrence Outcome

In the first large prospective comparative cohort study of recurrent glioblastoma Mukherjee et al. from St George's Hospital Atkinson Morley Wing, demonstrate that repeat resection confers a small but significant benefit in survival and quality of life over non-operative treatment. Best prognosis is associated with: younger age, KPS ≥ 80, late recurrence, MGMT promoter methylation, and EOR > 80 % [1].

Patients with recurrent glioblastoma (rGlioblastoma) have a poor prognosis, with survival ranging from 25 to 40 weeks. Antiangiogenic agents are widely used, showing a variable response.

In a study, Cardona et al., explored the efficacy of carmustine plus bevacizumab (BCNU/Bev) for treating rGlioblastoma.

They assessed 59 adult patients with histologically confirmed rGlioblastoma who were treated with BCNU/Bev as second-line regimen. The response rate (RR), progression free survival (PFS) and overall survival (OS) were evaluated according to their molecular expression profile, including CD133 mRNA expression, MGMT methylation (pMGMT), PDGFR amplification, YKL40 mRNA expression, IDH1/2 condition, p53 and EGFRvIII mutation status.

Median follow-up was 18.6 months, overall RR to the combination was 56.3%, and median PFS was 9.0 months (95% CI 8.0-9.9). OS from time of diagnosis was 21.0 months (95% CI 13.2-28.7) and from starting BCNU/Bev it was 10.7 months (95% CI 9.5-11.8). IDH1/2 mutations were found in 30.5% of the patients, pMGMT in 55.9% and high CD133 mRNA expression in 57.6%. Factors which positively affected PFS included performance status ($p = 0.015$), IDH+ ($p = 0.05$), CD133 mRNA expression ($p = 0.009$) and pMGMT+ ($p = 0.007$). OS was positively affected by pMGMT+ ($p = 0.05$). Meanwhile, YKL40 negatively affected PFS ($p = 0.01$) and OS ($p = 0.0001$). Grade ≥ 3 toxicities included hypertension (22%) and fatigue (12%).

BCNU/Bev is a safe and tolerable treatment for rGlioblastoma. Patients with MGMT+/IDH+ derive the greatest benefit from the treatment combination in the second-line setting. Nonetheless, high YKL40 expression discourages the use of antiangiogenic therapy [2].

In the series of Tejada y col., recurrence pattern was local only in 65.5 % of patients and non-local in 34.5 %. The univariate and multivariate analysis showed that greater preoperative tumor volume in T1 gadolinium enhanced sequences, was the only variable with statistical signification ($p < 0.001$) for increased rate of non-local recurrences, although patients with MGMT methylation and complete resection of enhancing tumor presented non-local recurrences more frequently. PFS was longer in patients with non-local recurrences (13.8 vs. 6.4 months; $p = 0.019$, log-rank). However, OS was not significantly different in both groups (24.0 non-local vs. 19.3 local; $p = 0.9$). Rate of non-local recurrences of patients treated with fluorescence guided surgery and standard radiochemotherapy was higher than previously published, especially in patients with longer PFS. Greater preoperative enhancing tumor volume was associated with increased rate of non-local recurrences [3].

Survival after repeat surgery was decreased in patients with recurrent Glioblastoma involving the subventricular zone SVZ at recurrence ($p = 0.022$). No other prognostic factors for survival after

repeat surgery were identified. This finding may have prognostic and therapeutic significance [4].

References

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