M8 Concomitant versus sequential Fotemustine and Bevacizumab in recurrent malignant gliomas: treatment response and survival outcomes in a retrospective analysis

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Background: Despite the standard therapy of newly-diagnosed maglignant gliomas (MGs), recurrence rate remains high (∼90%) and the treatment of recurrent MGs is still a clinical challenge. Nitrosoureas, mainly fotemustine (FTM), have been employed in monotherapy or in combination with other agents, including bevacizumab (BEV).

Materials and methods: We performed a retrospective analysis of 26 recurrent MGs patients (20 Glioblastoma multiforme and 6 Anaplasic gliomas) treated with concomitant or sequential FTM and BEV (cFTM/BEV and sFTM/BEV respectively) as second-line therapy after first-line with radio-chemotherapy as Stupp protocol. Efficacy was evaluated as median progression free survival (mPFS) and overall survival (mOS) with best response to MRI assessment (complete/partial response − CR, RP − and disease control rate − DCR). Subgroup analyses according to MGMT status were performed.

Results: Patients treated with the combination of FTM and BEV, both as concomitant and sequential scheme, had a mPFS of 9 months and a mOS of 11 months. Patients treated with cFTM/BEV (n = 13) experienced longer mPFS (8 vs 5 months; p = 0.2) and mOS (12 vs 6 months; p = 0.2) compared to sFTM/BEV patients (n = 13). PFS at 6 months was of 31% for sFTM/BEV and 62% for cFTM/BEV while PFS at 1 year was of 15% and 23% respectively. OS at 1 year was of 23% for both groups. With sFTM/BEV, RP was observed in 38% of patients with a DCR of 62%. With cFTM/BEV one CR (8%) and 9 RP (69%) were assessed with a DCR of 85%. Methylated MGMT patients (n = 12) had longer mPFS (11 vs 6 months; p = 0.2) and mOS (15 vs 6 months; p = 0.1) compared to unmethylated patients (n = 7) independently of type of treatment. Methylated patients treated with cFTM/BEV (n = 4) experienced longer mPFS (8 vs 5 months) and mOS (p = 0.08) compared to methylated patients treated with sFTM/BEV (n = 8).

Conclusion: In recurrent MGs the concomitant association FTM/BEV provide a survival and response benefit compared to sequential therapy FTM/BEV. Methylated patients experienced longer survival outcomes with the concomitant scheme of FTM/BEV.