ABSTRACT

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Sex-Dependent Analysis of Temozolomide-Induced Myelosuppression and Effects on Survival in a Large Real-life Cohort of Glioma Patients.

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OBJECTIVE: To investigate the association of radiochemotherapy-induced cytopenia with sex of glioma patients and its potential impact on survival.

METHODS: We retrospectively analyzed cytopenia during temozolomide-based concomitant radiochemotherapy (RCT) in 492 glioma patients. Histological grading, molecular pathology, surgical procedures, adjuvant chemotherapy subsequent to the RCT phase and overall survival (OS) were recorded. The extent of cytopenia was correlated with sex and outcome.

RESULTS: Treatment-induced severe cytopenia (leuko-, lympho-, neutro- and thrombocytopenia) was more frequent in women than men (44 vs. 18%, p-value 0.0002). In women with IDH-wildtype high-grade astrocytomas there was a negative correlation of severe cytopenia in general and thrombocytopenia in specific during temozolomide RCT with OS independent from other predictors (92 (77-111) vs. 73 (21-127) weeks, p-values <0.05). In men there was also a trend for this unfavorable effect. Additionally, severe cytopenia in all blood cell lineages correlated with reduced temozolomide dose exposure during RCT (all p-values <0.05 in the total cohort) and reduced dose exposure was independently associated with worse OS (hazard ratios for OS complete vs. reduced temozolomide dose in the total/female cohort: 0.66 (0.47-0.92) and 0.4 (0.24-0.69), p-values <0.05).

CONCLUSIONS: Our analysis of treatment-induced cytopenia in a large cohort of glioma patients (i) confirms that women are at higher risk and (ii) demonstrates an association of cytopenia in women with shortened survival.

CLASSIFICATION OF EVIDENCE: This study provides class II evidence that women with glioma treated with temozolomide-based concomitant radiochemotherapy have more frequent treatment-induced severe cytopenia than men and that severe myelosuppression correlates with worse OS in women.

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