Dose dense temozolomide in patients with recurrent high grade gliomas: The UK experience

Catherine Garcia, MD [1] • Rachael Morgan, PharmD [2] • Lindsey Gruber, PharmD [2] •

John Villano, MD, PhD [3]

[1]Medical Oncology, University of Kentucky • [2]Clinical Oncology Pharmacy, University of Kentucky •

[3]Departments of Internal Medicine, Neurology, Neurosurgery, University of Kentucky

Introduction:
There are limited treatment modalities after high grade gliomas recurrence with no known therapy providing a survival advantage. Dose dense temozolomide (TMZ) affects intracellular O(6)-methylguanine-DNA methyltransferase (MGMT) depletion with cell cycle modulation and is an accepted treatment option with limited investigations, which have been focused on glioblastoma. Prolonged exposure to TMZ may improve survival in patients with limited therapeutic options.

Methods:
Patients were selected retrospectively from our practice and were followed since the start of dose dense TMZ until death or change of therapy. Progression free survival was assessed from the last date of evaluation.

Results:
A total of 26 patients were reviewed, with a mean age of 46 years old. The preferred dose dense scheme was the 21/28 day regimen (69.23%), with 6 patients on daily TMZ scheme (23%). The majority of patients were classified histologically as WHO grade IV (69 %) with 31% classified as WHO grade III. All of our patients received standard of care prior to beginning alternative therapies. The median progression free survival was 6 months. Progression free survival at 6 months and 12 months was 50% and 15.38%, respectively. Only 4 patients developed adverse effects that required discontinuation of therapy. The most common adverse event during therapy was thrombocytopenia. The main cause for stopping treatment was death or admission to hospice care. MGMT methylation status was positive in 3 patients and was unknown in 77% of our study. Patients with IDH wildtype had higher frequency of progression (p=0.037). Optune device was used in 30% of the patients and 57% had a history of prior exposure to bevacizumab.

Discussion:
Our results demonstrate a benefit of dose dense TMZ after previous treatment with standard TMZ dosing. In addition we found no apparent increase in treatment-related toxicities and we are currently identifying genomic and clinical factors associated with response to dose dense TMZ. In summary, additional analysis on dose dense TMZ regimes are warranted, as treatment options are limited and have not demonstrated improved outcome.