



## Positive Quality Intervention: Temozolomide (Temodar®) for Glioblastoma Multiforme

**Description:** The purpose of this PQI is a summary of the process for initiating and monitoring oral temozolomide therapy in patients with Glioblastoma Multiforme (GBM).

**Background:** GBM is the most common primary malignant brain tumor in adults and comprises 54 % of all gliomas with a median survival of 6 to 12 months.<sup>1</sup> Temozolomide is an FDA approved medication used to treat GBM.<sup>2</sup> Temozolomide is a prodrug that is converted into its active alkylating metabolite which causes DNA double strand breaks and apoptosis.<sup>2</sup> Concurrent treatment with temozolomide and radiation followed by a 4 week break, then maintenance temozolomide for 5 days every 28 days for 6 cycles was found to improve 2 year survival from 10.4% (radiation alone) to 26.5% (radiation + temozolomide).<sup>3</sup> Furthermore, patients with MGMT promoter methylated GBM were shown to have a better 18-month overall survival with concurrent temozolomide and radiation (62%) when compared with unmethylated MGMT (8%).<sup>4</sup>

### PQI Process:

- Ensure appropriate indication and dose, keeping in mind that dose modifications occurred frequently in the clinical trials
  - Temozolomide 75 mg/m<sup>2</sup> PO daily during radiation followed by a 4 week break, then 150-200 mg/m<sup>2</sup> PO daily x 5 every 28 days for 6 cycles<sup>2</sup>
- Concurrent temozolomide with radiation can cause lymphocytopenia therefore ensure appropriate prophylaxis of Pneumocystis Jiroveci with oral trimethoprim-sulfamethoxazole, inhaled pentamidine, atovaquone or dapsone<sup>2</sup>
- Ondansetron should be prescribed for prevention and treatment of nausea and vomiting; if nausea and vomiting occurs, ondansetron may be taken 30-60 minutes prior to temozolomide<sup>2</sup>
- Monitor pregnancy, CBC (lymphopenia, thrombocytopenia), liver enzymes, pneumocystis<sup>2</sup>

### Dosing Interruption or Discontinuation during Concomitant Radiotherapy and Temozolomide<sup>2</sup>

Toxicity	Therapy Interruption	Discontinue
Absolute Neutrophil Count	≥ 0.5 x 10 <sup>9</sup> /L and < 1.5 x 10 <sup>9</sup> /L	< 0.5 x 10 <sup>9</sup> /L
Platelet Count	≥ 10 x 10 <sup>9</sup> /L and less < 100 x 10 <sup>9</sup> /L	< 10 x 10 <sup>9</sup> /L
Common Toxicity Criteria (CTC) Non-Hematological Toxicity (except for alopecia, nausea, vomiting)	CTC Grade 2	CTC Grade 3 or 4

### Temozolomide Dose Levels for Maintenance Treatment<sup>2</sup>

Dose level	Dose (mg/m <sup>2</sup> /day)	Remarks
-1	100	Reduction for prior toxicity
0	150	Dose during Cycle 1
1	200	Dose during Cycles 2-6 in absence of toxicity

### Temozolomide Dose Reduction or Discontinuation during Maintenance Treatment<sup>2</sup>

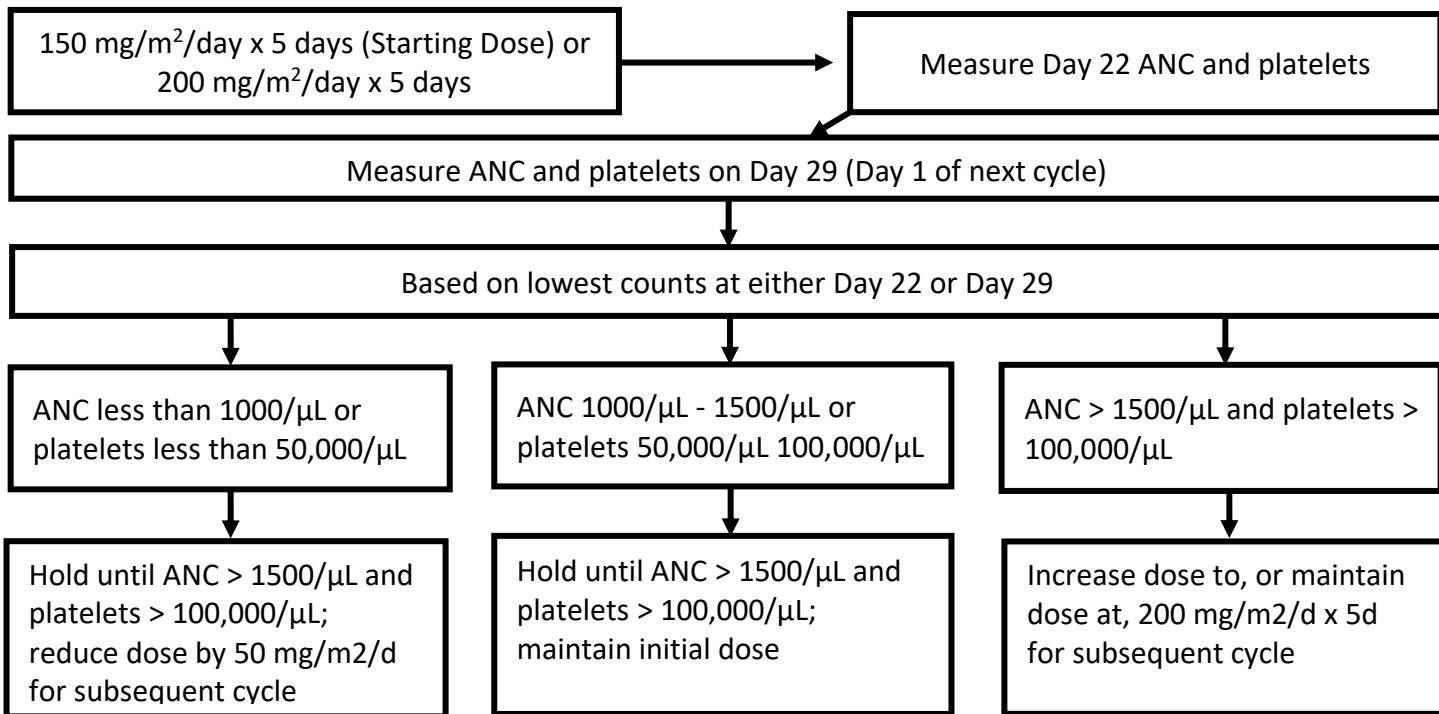
Toxicity	Reduce Temozolomide by 1 Dose Level	Discontinue
Absolute Neutrophil Count	Less than 1.0 x 10 <sup>9</sup> /L	Discontinue if dose reduction to < 100 mg/m <sup>2</sup> is

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Platelet Count	Less than $50 \times 10^9 /L$	required or if the same Grade 3 non-hematological toxicity (except for alopecia, nausea, vomiting) recurs after dose reduction
CTC Non-Hematological Toxicity (except for alopecia, nausea, vomiting)	CTC Grade 3	CTC Grade 4

**Temozolomide Dose Modification Table<sup>2</sup>**



**Patient Centered Activities:**

- Provide [Oral Chemotherapy Education \(OCE\) Sheet](#)
- Provide [Treatment Support Kit \(TSK\)](#)
- Counsel patient on disease state, treatment regimen, what to expect and verify patient understanding
- Counsel patient on common side effects which include alopecia, constipation, nausea/vomiting, headache, seizure, and fatigue
- Temozolomide is preferred to be taken one hour prior to radiation on radiation days
- Counsel patient to swallow capsules (may be multiple) whole with a full glass of water
  - May administer on an empty stomach and/or bedtime to reduce nausea/vomiting and consistently take in this manner
  - Do not repeat dose if vomiting occurs after the dose is administered

**References:**

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers.
2. [Temozolomide \[prescribing information\]](#).
3. Stupp R, Mason WP, van den Bent MJ, et al: Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 352:987-96, 2005.
4. Hegi ME, Diserens AC, Godard S, et al: Clinical trial substantiates the predictive value of O-6- methylguanine-DNA methyltransferase promoter methylation in glioblastoma patients treated with temozolomide. Clin Cancer Res 10:1871-4, 2004.

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