



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.¹ Temozolomide is an FDA approved medication used to treat GBM.² Temozolomide is a prodrug that is converted into its active alkylating metabolite which causes DNA double strand breaks and apoptosis.² 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).³ 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%).⁴

PQI Process:

- Ensure appropriate indication and dose, keeping in mind that dose modifications occurred frequently in the clinical trials
 - Temozolomide 75 mg/m² PO daily during radiation followed by a 4 week break, then 150-200 mg/m² PO daily x 5 every 28 days for 6 cycles²
- Concurrent temozolomide with radiation can cause lymphocytopenia therefore ensure appropriate prophylaxis of Pneumocystis Jiroveci with oral trimethoprim-sulfamethoxazole, inhaled pentamidine, atovaquone or dapsone²
- 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 temozolomide²
- Monitor pregnancy, CBC (lymphopenia, thrombocytopenia), liver enzymes, pneumocystis²

Dosing Interruption or Discontinuation during Concomitant Radiotherapy and Temozolomide²

Toxicity	Therapy Interruption	Therapy Discontinuation
Absolute Neutrophil Count	Greater than or equal to 0.5 and less than 1.5 x 10 ⁹ /L	Less than 0.5 x 10 ⁹ /L
Platelet Count	Greater than or equal to 10 and less than 100 x 10 ⁹ /L	Less than 10 x 10 ⁹ /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 Treatment²

Dose level	Dose (mg/m ² /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

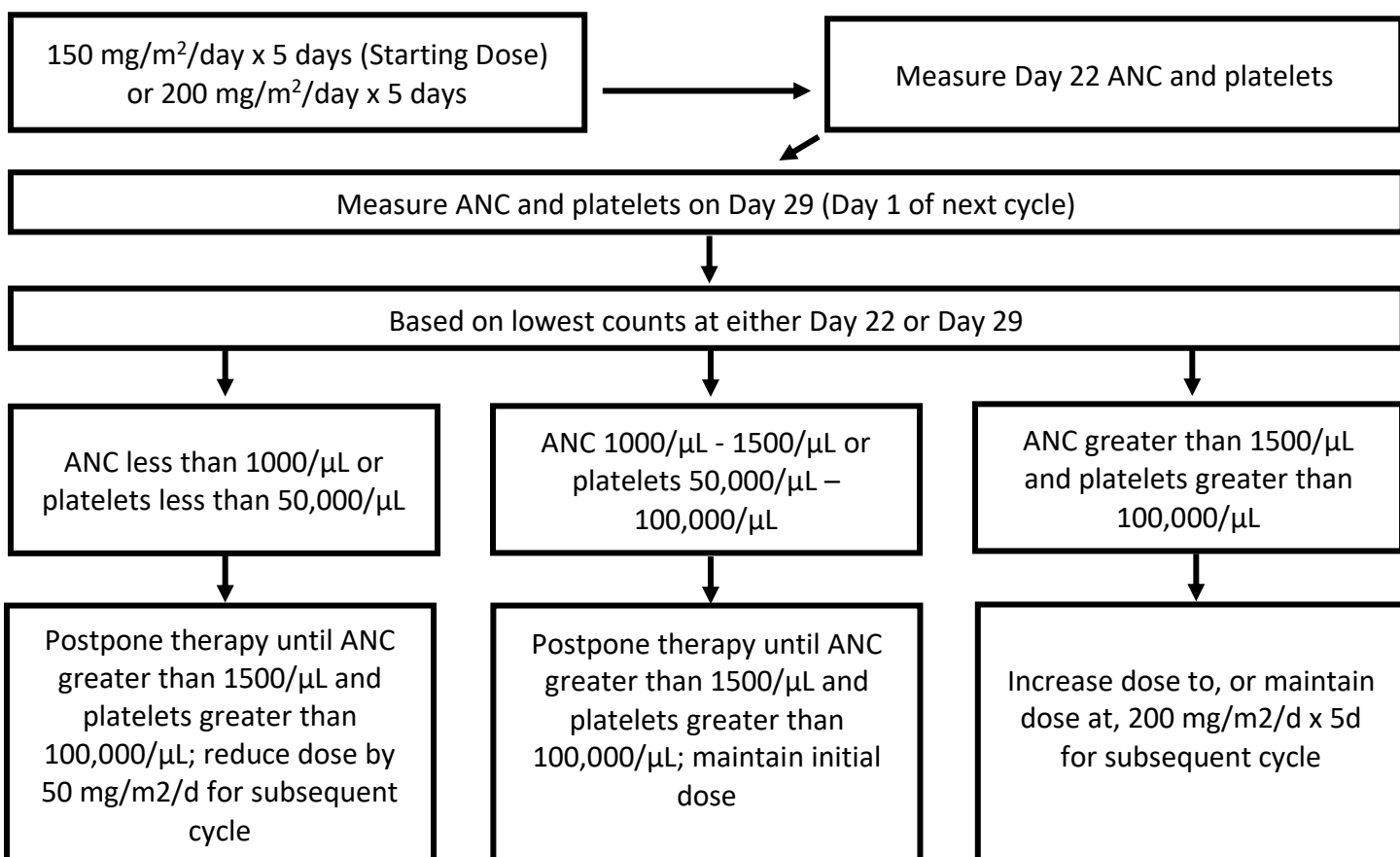
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Temozolomide Dose Reduction or Discontinuation during Maintenance Treatment²

Toxicity	Reduce Temozolomide by 1 Dose Level	Discontinue Temozolomide
Absolute Neutrophil Count	Less than $1.0 \times 10^9/L$	Discontinue if dose reduction to less than 100 mg/m^2 is required or if the same Grade 3 non hematological toxicity (except for alopecia, nausea, vomiting) recurs after dose reduction
Platelet Count	Less than $50 \times 10^9 /L$	
Common Toxicity Criteria (CTC) Non Hematological Toxicity (except for alopecia, nausea, vomiting)	CTC Grade 3	CTC Grade 4

Temozolomide Dose Modification Table²



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,

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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. V.2.2021, 09/08/21.
2. Temozolomide [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc.
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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