

FAST FACTS

N0577 - Phase III Intergroup Study of Radiotherapy with Concomitant and Adjuvant Temozolomide versus Radiotherapy with Adjuvant PCV Chemotherapy in Patients with 1p/19q Co-deleted Anaplastic Glioma or Low Grade Glioma

Pre-Registration Inclusion Criteria

1. Central pathology review submission
US and Canadian sites:
This review is mandatory prior to registration to confirm eligibility. Patients must be willing to submit tissue samples for mandatory central pathology review submission (see Sections 17.2 and 17.51). It should be initiated as soon after surgery as possible.
2. 1p/19q Co-deletion and IDH Mutation
Tissue must have been determined to have local 1p/19q co-deletion and IDH mutation prior to submission for central path review.
 - o Tumor tissue must show co-deletion of chromosomes 1p and 19q. For eligibility, the 1p/19q analysis results will be accepted from the local site, as determined by either a locally available or reference laboratory (for US, must be CLIA certified); Acceptable methods for determination of 1p/19q loss include fluorescent in-situ hybridization (FISH), by genomic sequencing or methylomic analyses. US and Canadian sites must send a copy of the official report to the pathology coordinator and upload it in Rave.
 - o Tumor must also show evidence of IDH mutation by immunohistochemistry or genomic analyses. This should be performed at the local site (US: performed in a CLIA certified laboratory). The site must send a copy of the official report to the pathology coordinator and upload it in Rave.

Registration Inclusion Criteria

1. Age
Age \geq 18 years of age.
2. Diagnosis
Newly diagnosed and \leq 3 months from surgical diagnosis. Patients not recently diagnosed (i.e. patients who had surgical procedure $>$ 3 months earlier) with grade 2 or 3 gliomas are eligible if the patient has not received prior radiation or prior chemotherapy. Patients cannot have received prior treatment directed at this neoplasm with the exception of prior surgery.
3. Histologic evidence of WHO Grade 2 or 3 oligodendroglioma, defined as a glioma with 1p/19q codeletion in combination with any IDH1 or IDH2 mutation. Codeletion and IDH status should be determined at the referring site's local or reference laboratory.
4. Patients with codeleted low grade gliomas must also be considered "high risk" by exhibiting one or more of the following characteristics:
 - Age \geq 40 and any surgical therapy
 - Age $<$ 40 with prior and subtotal resection or biopsy (i.e., anything less than gross total resection)
 - Documented growth following prior surgery (NOTE: patients with prior surgery cannot have received prior radiation, chemotherapy or targeted therapy)
 - Intractable seizures
5. Surgery
Surgery (partial or gross total resection or biopsy) must be performed \geq 2 weeks prior to registration; patient must have recovered adequately from the effects of surgery.
6. Laboratory Values

The following laboratory values obtained ≤ 21 days prior to registration.

- Absolute neutrophil count (ANC) ≥ 1500 /mm³
- Platelet (PLTs) count $\geq 100,000$ / mm³
- Hemoglobin (Hgb) > 9.0 g/dL
- Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN)
- SGOT (AST) ≤ 3 x ULN Creatinine ≤ 1.5 x ULN

7. Pregnancy Test

Negative serum or urine pregnancy test done ≤ 7 days prior to registration, for women of childbearing potential only.

8. Neurocognitive Tests and Quality of Life (QOL) Questionnaires

Willingness and ability to personally complete neurocognitive testing (without assistance) and willingness to complete the QOL testing, (either personally or with assistance) (see Section 4.3).

9. ECOG Performance Status

ECOG performance status (PS) of 0, 1 or 2 (See Appendix I).

10. Patient Informed Consent

Written informed consent.

11. Return to Enrolling Institution

Willingness to return to enrolling institution for follow-up during the Active Monitoring Phase (that is, the active treatment and observation portion) of the study). Patients who have been formally transferred to another active and approved site participating in this study would not need to return to the enrolling institution for this purpose.

12. Mandatory Tissue and Blood Samples for Correlative Research

Willingness to allow the provision of tissue samples for correlative research (see Sections 6.17, 17.3, and 17.52-17.53), as long as adequate tissues are available.

Patients will not be excluded from participation in the study, if they are willing to allow provision of tissues for the correlative research, but there are insufficient quantities of tissue for the correlative analyses (e.g., a patient otherwise eligible and willing who had biopsy only).

Willingness to allow the provision of blood samples for correlative research (see Sections 6.17 and 14.0). Patients are not excluded from participation in the study, if they are willing to provide the mandatory biospecimens for translational/correlative research, but for logistical reasons the specimen(s) were not obtainable or if the volume collected was insufficient.

13. Ability to read and comprehend English (or French for Canadian sites). For French-Canadian sites, please see [Section 4.3](#) for instructions on accessing French-translated patient materials.

Registration Exclusion Criteria

1. Fetal /Newborn Toxicity

This study involves agents that have known genotoxic, mutagenic and teratogenic effects, and thus the following categories are ineligible:

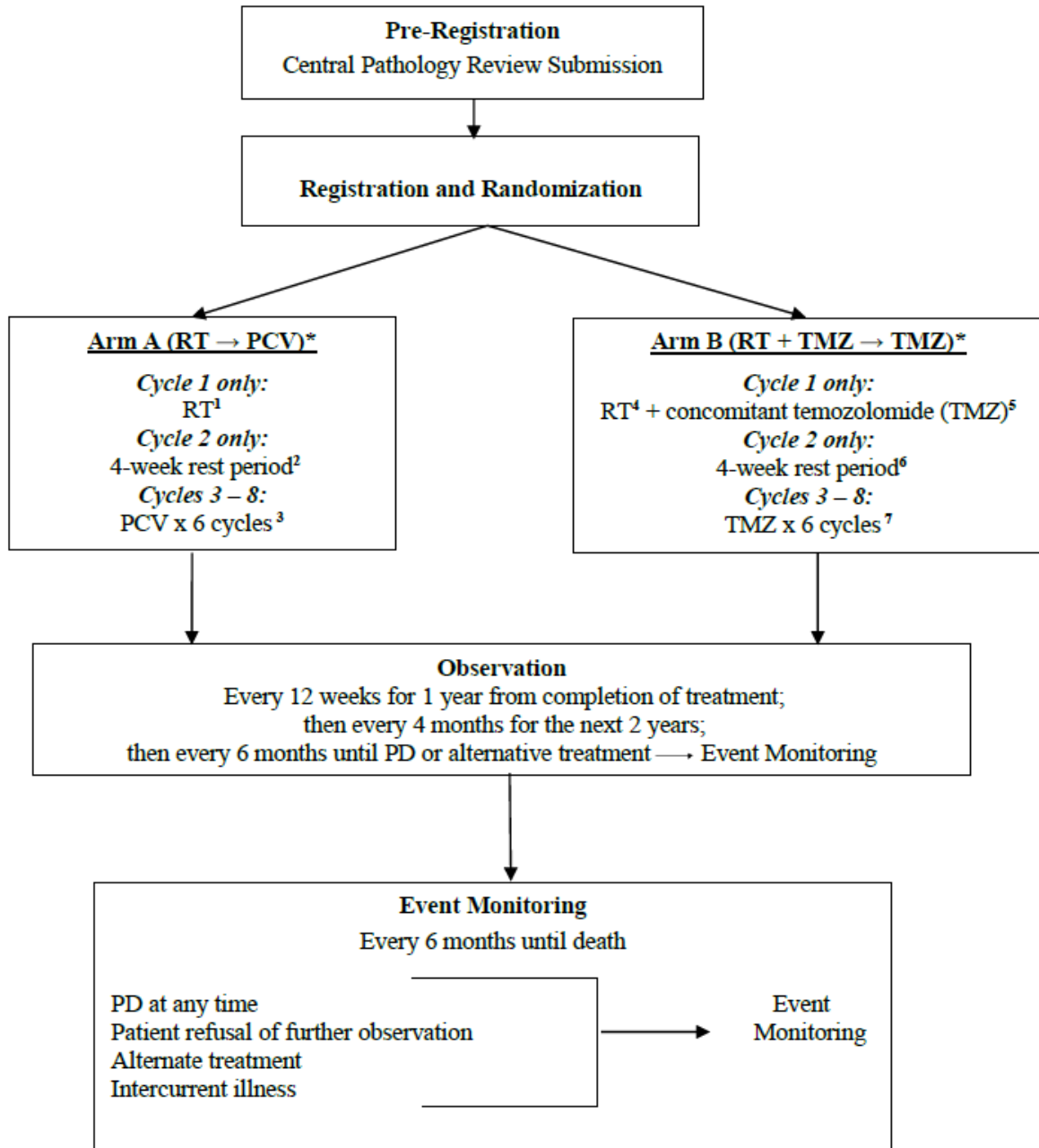
- Pregnant women
- Nursing women
- Men or women of childbearing potential who are unwilling to employ adequate contraception or contraceptive method during this study and 6 months following the completion of chemotherapy treatments.

2. Prior Treatment for a CNS neoplasm

History of prior radiation therapy or chemotherapy for glioma. **Note:** Patients who have a history of prior low grade glioma (with or without a distant history of prior surgery for that glioma), but

who have never received prior chemotherapy or radiation therapy for the glioma are eligible for the study as long as other criteria stated in 3.2 and 3.3 are met.

3. Concurrent Illness or Disease
 - a. Co-morbid systemic illnesses or other severe concurrent disease which, in the judgment of the investigator, would make the patient inappropriate for entry into this study or interfere significantly with the proper assessment of safety and toxicity of the prescribed regimens.
4. Immunocompromised Status
 - a. Concomitant serious immunocompromised status (other than that related to concomitant steroids) that would compromise the safety of the patient on the study.
5. HIV Positive Patients Receiving Retroviral Medications
 - a. Patients known to be HIV positive and currently receiving retroviral therapy are not eligible. **Note:** Patients known to be HIV positive, but without clinical evidence of an immunocompromised state, are eligible for the study
6. Uncontrolled Intercurrent Illness
 - a. Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
7. Other Investigational Agents
 - a. Receiving any other investigational agent that would be considered as a treatment for the primary neoplasm.
8. Other Active Malignancies
 - a. Other active malignancy within 3 years of registration. Exceptions: Non-melanotic skin cancer or carcinoma-in-situ of the cervix; patients with low-risk prostate cancer who do not require treatment per ESMO guidelines and under observation. **Note:** If there is a history of prior malignancy, the patient is not eligible if they are receiving other specific treatment (with the exclusion of hormonal therapy or Her-2 inhibitors) for their cancer or if they have received prior total body irradiation which included the brain.
9. Significant Cardiovascular History
 - a. History of myocardial infarction \leq 6 months, or congestive heart failure requiring use of ongoing maintenance therapy for life-threatening ventricular arrhythmias.
10. History of Hepatitis Infection
 - a. Recent history of hepatitis infection or if the treating physician determined that the patient would be at significant risk of reactivation of hepatitis.



* Patients who discontinue therapy for unacceptable adverse events or for reasons other than progression will go to observation until progression or starting alternative therapy. See [Section 13.7](#).