Cancer Research Consortium of West Michigan
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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 QAS.
   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 QAS.

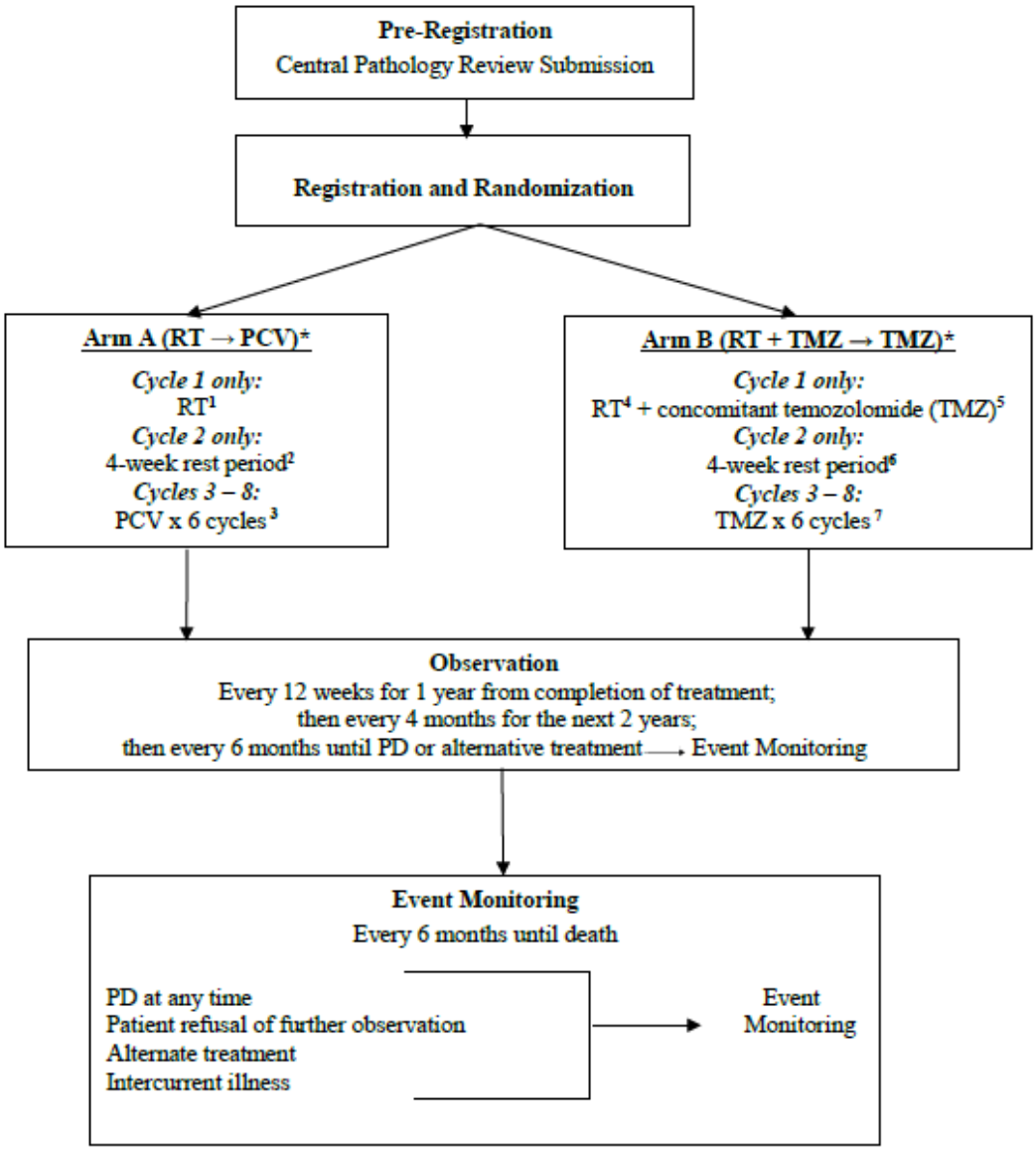
Registration Inclusion Criteria

1. Age
   Age ≥ 18 years of age.
2. Diagnosis
   Newly diagnosed and ≤ 3 months from surgical diagnosis. Patients are also eligible if they have had a prior surgical procedure > 3 months earlier for low grade glioma, as long as the patient has not received prior radiation or prior chemotherapy.
3. Histological evidence of WHO grade III anaplastic glioma or WHO grade II low grade glioma with locally diagnosed combined 1p/19q loss and the presence of an either IDH1 or IDH2, both as established by a local or referenced laboratory qualified for the study.
   Note: Mixed gliomas are eligible, regardless of the degree of astrocytic or oligodendrocytic predominance, as long as the tumor is also co-deleted for 1p and 19q.
4. Patients with codeleted low grade gliomas must also be considered “high risk” by exhibiting one or more of the following characteristics:
   • Age ≥ 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 ≥ 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 ≥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 specimens(s) were not obtainable or if the volume collected was insufficient.

SCHEMA

Please refer to the full protocol text for a complete description of the treatment plan and follow-up requirements.



* 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.