Cleveland Clinic

Vorinostat, Temodar & RT for Newly Diagnosed GBM CC827/ABTC 0902

Full Title
Phase I/II Study of Vorinostat (Suberoylanilide Hydroxamic Acid [SAHA]), Temozolomide, and Radiation Therapy in Patients with Newly Diagnosed Glioblastoma.

Principal Investigator
Manmeet Ahluwalia, MD

Contact Information
Cathy Schilero, RN, BSN
216.444.4068

Eligibility
Inclusion

- Central pathology review submission. This review is mandatory prior to registration to confirm eligibility. It should be initiated as soon after surgery as possible.
- Treatment should begin ≥2 weeks and ≤5 weeks following surgery.
- ≥18 years of age.
- Histologically confirmed glioblastoma multiforme as determined by preregistration central pathology review. NOTE: Gliosarcomas and other grade 4 astrocytoma variants (e.g., giant cell) are eligible.
- Bidimensionally measurable or evaluable disease by gadolinium MRI or contrast CT scan.
- Must begin partial brain radiotherapy on the same day that vorinostat and temozolomide begin. NOTE: Radiotherapy guidelines are detailed in Section 7.1.
- Karnofsky performance status of >60 (Appendix II) or ECOG performance score 0, 1, or 2 (Appendix V). The same scoring system should be used throughout the study.
- The following laboratory values obtained ≤14 days prior to registration.
  • ANC ≥1500
  • PLT ≥100,000
  • WBC ≥3000
  • HgB ≥10.0 g/dL – NOTE: This level may be reached by transfusion.
  • Total bilirubin ≤2.0 x UNL
  • SGOT (AST) ≤2 x UNL
  • Creatinine ≤1.5 mg/dL
- Life expectancy ≥12 weeks.
- Negative serum pregnancy test done ≤7 days prior to registration, for women of childbearing potential only.
- For Phase I established MTD and Phase II patients only: Willing and able to complete neurocognitive (see Section 4.2).
- Ability to provide informed written consent.
- Willingness to return to NCCTG or ABTC enrolling institution for follow-up.
  Phase I established MTD patients (Section 7.27, second paragraph) and Phase II patients: Willing to provide mandatory tissue samples (slides or blocks) for research purposes (see Sections 6.36 and 17.4)
- Willing to forego *other* cytotoxic and non-cytotoxic drug therapy against the tumor while being treated with vorinostat and temozolomide.

Exclusions

- Any of the following:

• Pregnant women
• Nursing women
• Men or women of childbearing potential who are unwilling to employ adequate contraception throughout the duration of the study and for 12 weeks after treatment has ended.

NOTE: Vorinostat is an investigational agent whose genotoxic effects on the developing fetus and newborn are unknown.

- Prior cytotoxic drug therapy, non-cytotoxic drug therapy, or experimental drug therapy for brain tumors.
- Prior cranial RT.
- Prior Gliadel wafers.
  Known hypersensitivity to any of the components of vorinostat or other agents used in study.
- Valproic acid, another histone deacetylase inhibitor, ≤2 weeks prior to registration and during treatment.
- Other active malignancy ≤3 years prior to registration. EXCEPTIONS: Nonmelanotic skin cancer or carcinoma-in-situ of the cervix. NOTE: If there is a history of prior malignancy, they must not be receiving other specific treatment