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.

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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 \( \geq 2 \) weeks and \( \leq 5 \) weeks following surgery.
- \( \geq 18 \) 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 \( \leq 14 \) days prior to registration.
  - ANC \( \geq 1500 \)
  - PLT \( \geq 100,000 \)
  - WBC \( \geq 3000 \)
  - HgB \( \geq 10.0 \) g/dL – NOTE: This level may be reached by transfusion.
  - Total bilirubin \( \leq 2.0 \times \text{UNL} \)
  - SGOT (AST) \( \leq 2 \times \text{UNL} \)
  - Creatinine \( \leq 1.5 \) mg/dL
- Life expectancy \( \geq 12 \) weeks.
- Negative serum pregnancy test done \( \leq 7 \) 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