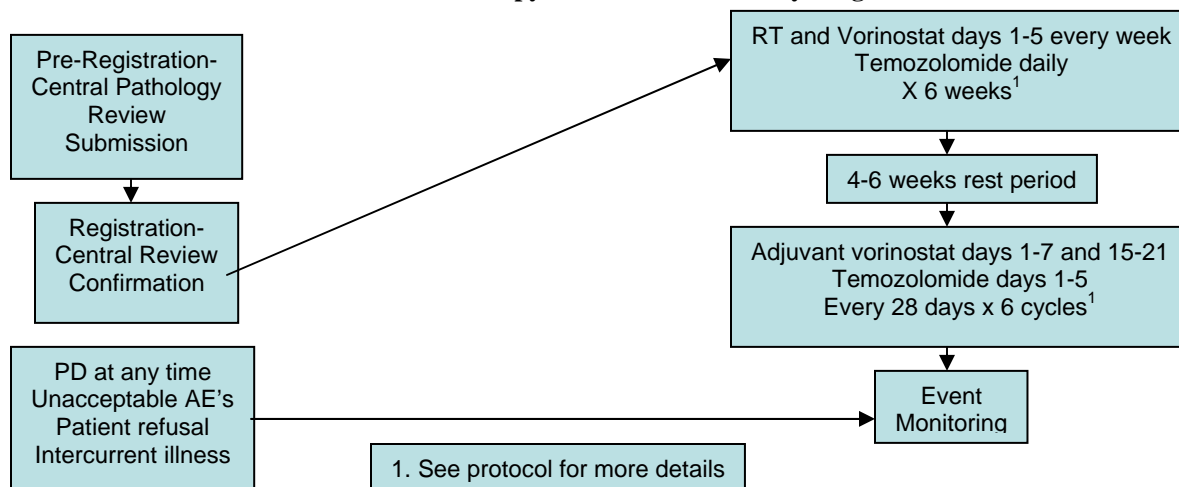


N0874- Phase I/II Study of Vorinostat (Suberoylnilide Hydroxamic Acid [SAHA]), Temozolomide and Radiation Therapy in Patients with Newly Diagnosed Glioblastoma



This is a Phase I/Phase II study looking at the use of Vorinostat in combination with RT and TMZ in newly diagnosed GBM patients. The study will also look at the use of maintenance Vorinostat in combination with TMZ for 6 cycles.

Major Inclusion Criteria

- Histologically confirmed newly diagnosed GBM 1. Mandatory central pathology review to confirm diagnosis.
- Bidimensionally measurable or evaluable disease by gadolinium MRI or contrast CT.
- Must begin partial brain RT on the same day as vorinostat and TMZ begin.¹
- ECOG PS of 0, 1, or 2 or Karnofsky score ≥ 60 .
- Adequate hematologic values (Hgb ≥ 10 g/dL; ANC ≥ 1500 ; WBC ≥ 3000 ; PLT $\geq 100,000$).
- Adequate renal function (crt ≤ 1.5 mg/dL); and liver function (SGOT/AST ≤ 2 x ULN; total bili ≤ 2.0 x ULN).
- Life expectancy ≥ 12 weeks.
- Phase I established MTD and Phase II patients only:
 - Willing and able to complete neurocognitive tests.
 - Willing to provided mandatory tissue samples for research purposes.
- Willing to forego other cytotoxic and non-cytotoxic drug therapy for their GBM while on study.
- Ability to take oral medication.
- Not receiving any other investigational agent as treatment for the primary neoplasm.

Major Exclusion Criteria

- No pregnant or nursing women.
- Prior cytotoxic, non-cytotoxic 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 the study.
- Valproic acid ≤ 2 weeks prior to registration and during treatment.
- Other active malignancy ≤ 3 years prior to registration¹.
- Uncontrolled infection.
- Immunocompromised patients and patients known to be HIV positive and currently receiving antiretroviral therapy¹.
- Co-morbid systemic illness or other severe concurrent disease which in the judgment of the investigator would make the patient inappropriate for study entry¹.
- Uncontrolled intercurrent illness or psychiatric illness/social situation that would limit compliance with study requirements.
- History of MI or unstable angina ≤ 6 months prior to registration, or CHF requiring use of ongoing maintenance therapy or life-threatening ventricular arrhythmias.
- Congenital long QT syndrome or prolonged QTc interval (>450 msec).
- Any Category I drugs that are generally accepted to have a risk of causing Torsades de Pointes ≤ 7 days prior to registration¹.

1. See protocol for more specific details.