Alliance A071102: A Phase II/III Randomized Trial of Veliparib or Placebo in Combination with Adjuvant Temozolomide in Newly Diagnosed Glioblastoma with MGMT Promoter Hypermethylation

Fast Facts

Patient Selection

1. On-study guidelines

Although they will not be considered formal eligibility (exclusion) criteria, physicians should recognize that the following may seriously increase the risk to the patient entering this protocol:

- Psychiatric illness which would prevent the patient from giving informed consent.
- Medical condition such as uncontrolled infection (including HIV), uncontrolled diabetes mellitus or cardiac disease which, in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient.
- Patients with uncontrolled infection or patients with HIV with immunosuppression should be definitively excluded.
- Patients with a "currently active" second malignancy other than non-melanoma skin cancers. Patients are not considered to have a "currently active" malignancy if they have completed therapy and are free of disease for ≥ 3 years. Patients treated for prior brain tumor, nasopharynx or sinus cancer with a previous course of radiation in which significant dose to the brain was delivered may not participate in this trial.
- Patients who cannot swallow oral formulations of the agent(s).
- Women and men of reproductive potential should agree to use an appropriate method of birth control throughout their participation in this study due to the teratogenic potential of the therapy utilized in this trial. Appropriate methods of birth control include abstinence, oral contraceptives, implantable hormonal contraceptives or double barrier method (diaphragm plus condom).

2. Pre-Registration Eligibility Criteria

a. Histologic documentation: Newly diagnosed WHO Grade IV intracranial glioblastoma or gliosarcoma. GBM with oligodendroglial features are NOT PERMITTED in this study if they are 1p19q codeleted. Sites submitting GBM with oligodendroglial features will be asked to provide results of 1p/19q codeletion status.
b. Sufficient tissue available for central pathology review and MGMT methylation status evaluation.
c. Age ≥ 18 years of age
d. Patients who have had a local MGMT testing that is unmethylated are not allowed to participate.

3. Registration Eligibility Criteria

a. Tumor MGMT promoter hypermethylation determined by central testing at MD Anderson.
b. Confirmation by central pathology review of WHO Grade IV glioblastoma or gliosarcoma.
c. Required Initial Laboratory Values: (Within 14 days prior to study registration)

- Absolute neutrophil count (ANC) ≥ 1500 cells/mm3
- Platelets ≥ 100,000 cells/mm3
- Creatinine ≤ 1.5x ULN
- Bilirubin * ≤ 1.5x ULN
- ALT ≤ 3 x ULN
- AST ≤ 3 x ULN

*Unless patient has Gilbert's disease

d. ECOG Performance Status ≤ 2
e. Measurable disease and/or non-measurable disease as defined in Section 11.0.
   - Extent of resection: Patients with complete resection, partial resection, or biopsy are eligible.
f. Progression: Patients deemed to have progressive disease based on clinical deterioration after chemoradiation or radiographic progression outside of the radiation field are not eligible. (See Section 11.4.3.2 for definition of clinical deterioration). Patients deemed to have pseudoprogression (as defined in Section 11.4.3.2) are eligible.

4. Prior Treatment

a. Must have completed standard radiotherapy and concomitant TMZ therapy as defined in Appendix I and determined by the study oncologist.

b. Besides concomitant TMZ with radiation, no other therapy (neo-adjuvant or adjuvant) can be given prior to study registration, including chemotherapy (also including Gliadel/BCNU wafers), biologics, immunotherapy, or radiation therapy. The only exception is the Optune device (NovoTTF-100A), which may be started any time after end of radiation therapy up through the initiation of Cycle 1. Intent to use Optune must be declared at registration for stratification (see Sections 4.4 and 4.8). See Sections 5.0 and 8.1.11 for additional requirements.

c. Not pregnant and not nursing, because this study involves an agent that has known genotoxic, mutagenic and teratogenic effects. Females of childbearing potential must have negative urine or serum pregnancy test within 7 days of registration but before start of treatment. A female of childbearing potential is a sexually mature female who: 1) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 12 consecutive months (i.e., has had menses at any time in the preceding 12 consecutive months).

5. Concomitant Medications:

a. Patients receiving anticoagulation should be on stable dose 2 weeks prior to registration.

6. ***Comorbid Conditions: Patients are unable to participate due to the following:***
    a. Seizure disorder that is uncontrolled at the time of registration. The definition of controlled seizures is patients must be without seizures for at least 10 days prior to registration.
    b. Grade 3 or 4 thromboembolic disease within 6mo of registration
    c. Known history of prolonged QT syndrome

7. ***No history of major surgery ≤ 14 days prior to registration***

Treatment:

Protocol therapy will consist of 6 cycles administered on days 1-7 of each 28 day cycle. Treatment will continue until disease progression or unacceptable adverse event or maximizing the dose reductions, for a maximum period of 6 cycles.

Agent	Dose	Route	Day	ReRx
temozolomide	150-200 mg/m2	PO	Day 1-5	every 28 days
veliparib or placebo	40 mg bid	PO	Day 1-7	every 28 days

Pre-study Parameters

- History and physical, weight, PS, Height
- Pulse, Blood Pressure
- Fatigue/Uniscale Assessment (See Appendix IV)
- Mini Mental State Examination (See Appendix V)
- Complete Blood Count, Differential, Platelets
- Serum Creatinine,
- Albumin, glucose
- AST, ALT, Alk. Phos., Bili
- Serum or Urine HCG
- Central Pathology review and MGMT testing for eligibility
- Brain Imaging (MRI or CT)
- Blood Samples