A Prospective, Multi-institutional Phase II Trial Evaluating Temozolomide vs. Temozolomide and Olaparib for Advanced Pheochromocytoma and Paraganglioma

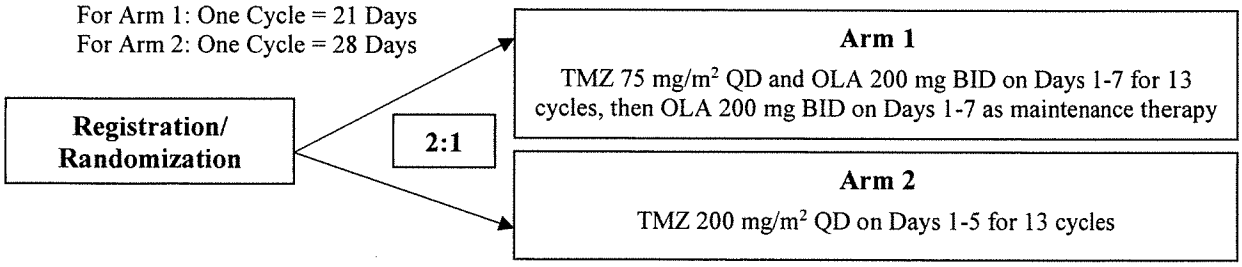
Eligibility Criteria (see Section 3.0)

- Histologically-proven advanced (metastatic or unresectable primary) pheochromocytoma or paraganglioma
- Radiographic evidence of disease progression by RECIST v1.1 criteria in the 12 months prior to registration
- Measurable disease as defined in Section 11.0
- Prior treatment with other chemotherapy, radiotherapy, or surgery must be completed ≥ 28 days prior to registration. Patients must have recovered from any effects of any major surgery prior to registration.
- Prior treatment with radiolabeled MIBG must be completed ≥ 12 weeks prior to registration; lifetime cumulative ^{131}I-MIBG dose must be < 1000 MBq kg^{-1}
- Prior treatment with antibiotics must be completed ≥ 7 days prior to registration
- No prior treatment with temozolomide, dacarbazine, or a PARP inhibitor
- No prior allogeneic bone marrow transplant or dUCBT.
- Not pregnant and not nursing; negative pregnancy test required ≤ 7 days prior to registration
- Women must use two highly effective forms of contraception during and for 1 month after treatment; male patients must use a condom during and for 3 months after treatment; see Section 3.2.5.
- Age ≥ 18 years
- ECOG Performance Status: 0-2
- No indication of uncontrolled, potentially reversible cardiac condition(s) as determined by investigator and no known congenital long QT syndrome.
- No extensive bilateral lung disease or pneumonitis.
- No abnormal organ or bone marrow function ≤ 28 days prior to registration
- Patients with HIV positivity allowed if CD4 Count > 250 cells/μL and undetectable viral load ≤ 6 months of reg.
- No active infection
- No history of myelodysplastic syndrome or acute myeloid leukemia
- No known gastrointestinal condition(s) that might predispose for drug intolerability or poor drug absorption
- No known medical condition causing an inability to swallow oral formulations of agents
- No history of allergic reaction attributed to compounds of similar composition to PARP inhibitors
- Concurrent use of combination antiretroviral therapy not permitted
- Chronic concomitant treatment with strong or moderate CYP3A4 inducers or inhibitors is not allowed; patients must discontinue the agent(s) ≥ 21 days prior to registration; enzalutamide and/or phenobarbital must be discontinued ≥ 5 weeks prior to registration

Required Initial Laboratory Values:
Absolute Neutrophil Count: ≥ 1500/mm^3
Platelet Count: ≥ 100,000/mm^3
Hemoglobin: ≥ 10 mg/dL*
Total Bilirubin: ≤ 1.5 x ULN**
AST/ALT: ≤ 3.0 x ULN
Creatinine: < 1.5 x ULN
OR
Calc. Creatinine Clearance: > 50 mL/min***

*In the absence of transfusion within the previous 24 hours
**Except in the case of Gilbert's syndrome, then Total Bilirubin must be ≤ 3.0 x ULN
***Calculated by Cockcroft-Gault equation

Schema



Treatment for Arm 1 patients will consist of temozolomide and olaparib for 13 cycles followed by continuation of olaparib alone as maintenance therapy or until disease progression, unacceptable adverse event, or withdrawal of consent. Treatment for Arm 2 patients will consist of temozolomide alone for 13 cycles or until disease progression, unacceptable adverse event, or withdrawal of consent. Patients will be followed for 5 years or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

Treatment must be administered and imaging must be conducted at the registering institution.

If the Group credited for enrollment is a non-Alliance Group, then other requirements from the credited Group may apply.