ACTR-41. A PHASE II, SINGLE ARM STUDY OF OPTUNÉ® IN BEVACIZUMAB-NAIVE SUBJECTS WITH RECURRENT WHO GRADE III MALIGNANT GLIOMA  
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There is an unmet clinical need for the treatment of progressive or recurrent anaplastic astrocytoma (World Health Organization [WHO] grade III) with poor median survival despite available chemotherapy. Published literature indicates that targeting extracellular tumor creating fields (ETTF) in malignant gliomas to selectively kill or arrest growth in glioma cell lines. The Optune® system is a novel non-invasive therapy approved by the FDA in 2011 for the treatment of recurrent supratentorial glioblastoma (GBM) (WHO grade IV) based on the results of a phase 3 clinical trial comparing TTF monotherapy with physician’s choice chemotherapy in patients with recurrent GBM demonstrating comparable overall survival and improved quality of life. No data is currently available on the response of WHO grade III malignant glioma to this technology. In addition, no biomarker is yet available in order to predict which patients will have a better response to the Optune® technology. This is a phase 2, single arm study in patients with WHO grade III malignant glioma who had progressive disease during first-line treatment with radiation, temozolomide (TMZ) and/or procarbazine/lomustine/vincristine (PCV) and who have not previously received bevacizumab (BEV) or any experimental agents. All patients are provided with the Optune® device. Frequency and duration of treatments are conducted in vitro. This is a prospective, open-label study. The primary objective will be to determine the efficacy of Optune® in recurrent malignant glioma patients (6-month progression-free survival). The secondary objectives will be to evaluate the safety and efficacy of Optune® in the subject population and to see if the presence of 1p19q codeletion correlates. RESULTS: To date, 6 patients (3 male) with a median age of 60.4 years (range 27.5–70.2 years) and median KPS of 70 (range 60–100%) have been enrolled. Histology includes 3 recurrent WHO grade II atypical and 3 recurrent WHO grade III anaplastic gliomas. Median number of recurrences was 5 (range 2–12). All 6 patients received bevacizumab and radiation. Median PFS was 3.3 months (range 1.0–4.6 months). Best radiographic response was SD (n=4) and PD (n=2); no patient achieved PR or CR. Treatment was well tolerated with no grade 3, 4, or 5 toxicities. Notable toxicities at least possibly related to treatment include grade 2 skin ulceration (n=2), grade 2 fatigue (n=1), and grade 1 fatigue (n=1). Five patients discontinued treatment due to disease progression; one patient withdrew consent. Median duration of the treatment was 3.7 months (range 1.0–4.6 months). CONCLUSIONS: In this heavily pretreated population, 4 of 6 patients attained SD with Optune treatment. Trial accrual is ongoing.

ACTR-42. CLINICAL TRIALS OF VAL-083 IN PATIENTS WITH CHEMORESISTANT GLIOBLASTOMA  
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Glialbloma (GBM) is the most common CNS-tumor. Patients with recurrent GBM have few treatment options and dismal prognosis. O6-methylguanine-DNA-methyltransferase (MGMT) is correlated with resistance to standard-of-care treatment with temozolomide and poor patient outcomes. Data from the ongoing ACTR-42 (NCT02871304) is a phase I clinical trial studying VAL-083 in recurrent GBM after failing temozolomide and bevacizumab, suggesting potential of VAL-083 to offer clinically meaningful survival benefits and a promising new treatment for GBM patients who have failed or are unlikely to respond to currently available chemotherapeutic regimens. In this phase II trial, VAL-083, 40 mg/m2/day x 3 every 21 days was well tolerated and was selected for study in subsequent clinical trials in GBM. These trials include i) a pivotal, randomized Phase 3 study measuring survival outcomes compared to “physician’s choice” control, which, if successful, would serve as the basis for a New Drug Application (NDA) submission for VAL-083. The control arm will consist of a limited number of salvage chemotherapies currently utilized in bevacizumab-failed GBM. ii) A non-comparative, biomarker-driven, open label study.iii) A single-arm Phase 2b study to confirm the tolerability of DelMar’s dosing regimen in combination with radiotherapy and to explore the activity of VAL-083 in newly diagnosed MGMT-unmethylated GBM patients whose tumors are known to express high MGMT levels. Trial designs and further details will be presented at the meeting. The results of these studies may support a new treatment paradigm in chemotherapeutic regimens for the treatment of GBM.

ACTR-43. PILOT STUDY OF OPTUNE® (NIVO-TTF-100A) FOR RECURRENT ATYPICAL AND ANAPLASTIC MALIGNIGIA  
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OPTUNÉ® is an oral small molecule inhibitor of c-Met. Bevacizumab produces...