Title

ACTR-41. A PHASE II, SINGLE ARM STUDY OF OPTUNE® IN BEVACIZUMAB-NAIVE SUBJECTS WITH RECURRENT WHO GRADE III MALIGNANT GLIOMA

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SION: CED of ACNU can be safely performed with real-time MRI monitoring when performed along with tumor resection. ACNU appears to have a favorable risk-benefit profile when delivered with CED.

ACTR-41. A PHASE II, SINGLE ARM STUDY OF OPTUNE® 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 glioma (World Health Organization [WHO] grade III) with poor median survival despite available chemotherapy. Published literature indicates that targeting mitosis via tumor treating fields (TTF) in rapidly dividing cancer cells by disrupting both spindle formation and normal cytokinesis selectively kills or arrests growth in glioma cell lines. The Optune® system is a novel anti-mitotic cancer therapy approved by the FDA in 2011 for the treatment of recurrent (supratentorial) glioblastoma (GB) (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 GB 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 have 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 titration experiments 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 LOH, and/or IDH1 mutation, confers a better response to Optune®.

ACTR-42. CLINICAL TRIALS OF VAL-083 IN PATIENTS WITH CHEMORESISTANT GLIOBLASTOMA

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Glioblastoma (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. Dianhydrogalactitol (VAL-083) is a bi-functional alkylating agent that readily crosses the blood-brain barrier and has demonstrated MGMT-independent activity in multiple GBM cell-lines and cancer stem cells, in vitro. VAL-083 showed promise against CNS-tumors in prior NCI-sponsored clinical trials. We recently concluded a phase I/II 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 I/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, Phase 2 study to determine if treatment of MGMT-unmethylated recurrent GBM with VAL-083 improves overall survival at 9 months, compared to reported CCNU control in bevacizumab-naïve patients. iii) A single arm Phase 2 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 (NOVOTTF-100A) FOR RECURRENT ATYPICAL AND ANAPLASTIC MENINGIOMA

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BACKGROUND: Medical therapies for surgery and radiotherapy-refractory meningiomas are limited. Optune (NovoTTF-100A) is an external cranial device that produces low intensity, intermediate frequency, alternating electric fields that interfere with cell division and stunt tumor cell growth. Although it is FDA-approved for use in recurrent glioblastoma, its efficacy in recurrent meningioma is unknown. METHODS: We conducted a pilot study for patients with recurrent atypical and anaplastic meningioma (WHO grades II–III). Optune is initiated as monotherapy for ≥ 18 hours per day per the established treatment standard. MRI scans are performed every 8 weeks. The primary endpoint is the 6-month progression-free survival (PFS) rate, with secondary endpoints of time to progression, radiographic response, safety and tolerability, overall survival (OS) rate, and volumetric and MR-perfusion correlates. RESULTS: To date, 6 patients (3 female) 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. Histologies include 3 recurrent WHO grade II atypical and 3 recurrent WHO grade III anaplastic meningiomas. Median number of recurrences was 5 (range 2–12). All patients had failed prior surgery 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-44. TREATMENT OUTCOMES IN ELDERLY PATIENTS WITH GLIOBLASTOMA: THE CLEVELAND CLINIC EXPERIENCE

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BACKGROUND: Fifty percent of glioblastoma patients are ≥ 65 years old. There is limited literature on outcomes of these patients. We report our experience with elderly patients with glioblastoma treated at our tertiary care center. METHODS: With IRB approval, the Cleveland Clinic's database was used to identify glioblastoma patients treated through 2000 - 2015. Overall survival (OS) from the diagnosis of glioblastoma was the primary end point. Cox proportional hazard models with stepwise variable selections were used for data analysis. RESULTS: 567 patients with a median age of 73 years (range, 65- 96 years), 57% of whom were male, were analyzed. Among 115 patients with known MGMT status, 54% were MGMT methylated. Twenty-eight percent of all patients underwent GTR (gross total resection), 28.8% had STR (sub-total resection) and 43.2% underwent biopsy. At diagnosis, 64% received chemoradiation, 34% underwent radiation and 2% received chemotherapy. The median OS and PFS (progression free survival) were 7.11 months (95% CI: 6.26, 8.65) and 4.0 months (CI: 3.6–4.5) respectively. The OS in MGMT-methylated patients was 12.85 months versus 8.46 months in MGMT-unmethylated ones (p 0.098). Patients with STR or biopsy had a higher risk of death and progression compared to GTR patients (p <0.001). The chemoradiation group had better PFS and OS compared to radiation alone; 6.197 versus 3.213 months (HR: 0.47, CI: 0.37 – 0.59, p <0.001) and 11.48 vs. 5.02 months (HR: 0.44, CI: 0.34 – 0.56, p <0.001) respectively. This effect was more evident in MGMT methylated patients; the chemoradiation group had a significantly higher OS than RT group 17.9 vs. 5.34 months (HR: 0.22, CI: 0.07 - 0.65, p 0.006) consistent with the recently reported Phase III study. CONCLUSIONS: Aggressive treatment with chemoradiation is associated with better outcomes in elderly GBM, particularly in MGMT methylated population.

ACTR-45. A PHASE IB STUDY EVALUATING THE C-MET INHIBITOR INC280 IN COMBINATION WITH BEVACIZUMAB IN GLIOBLASTOMA MULTIFORME (GBM) PATIENTS

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BACKGROUND: The HGF/c-MET pathway is deregulated in cancer affecting tumor cell proliferation, invasion, metastasis and angiogenesis. INC280 is an oral small molecule inhibitor of c-Met. Bevacizumab produces