Title

PHASE II TRIAL OF VACCINE IMMUNOTHERAPY IN PRIMARY GLIOBLASTOMA: ADJUNCTIVE AUTOLOGOUS DENDRITIC CELLS PULSED WITH LYSATE FROM IRRADIATED SELF-RENEWING AUTOLOGOUS TUMOR CELLS (AV-GBM-1)

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ceeded the minimum required for interim analysis in the heavily pretreated cohort. Among 30 patients, 4 achieved SD > 6 months (medulloblastoma, anaplastic ependymoma, myxopapillary ependymoma, metastatic atypical meningioma). Safety profile (related AEs): grade 3 = 7; grade 4 = 1. Most frequent grade 3-5 AEs regardless of attribution: tumor progression (6); anemia, hydrocephalus, lymphopenia (3 each); cerebral edema, headache (2 each). CONCLUSION: DCR exceeded the "go" boundary (i.e., > 2) in the heavily pretreated cohort. Nivolumab showed safety profile consistent with other studies. This cohort will continue to stage 2 and complete total accrual of 75 patients. The trial is currently being expanded to 10 additional sites across the BTTC/NCI-CONNECT consortium.

CTIM-33. PHASE II TRIAL OF VACCINE IMMUNOTHERAPY IN PRIMARY GLIOBLASTOMA: ADJUNCTIVE AUTOLOGOUS DENDRITIC CELLS PULSED WITH LYSATE FROM IRRADIATED SELF-RENEWING AUTOLOGOUS TUMOR CELLS (AV-GBM-1)

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In primary glioblastoma (GBM), overall survival (OS) is poor despite standard aggressive therapy. Adjunctive AV-GBM-1 vaccine immunotherapy may improve OS. In this multi-institutional phase II trial, key eligibility criteria for intent-to-treat (ITT) enrollment were: (1) primary GBM, (2) age < 70 years when GBM was resected, (3) successful GBM cell culture, (4) successful monocyte collection by leukapheresis, (5) KPS > 70 post-surgery, and (6) plan to treat with concurrent RT/TMZ. Dendritic cells (DC) were differentiated from monocytes by culturing in IL-4 and granulocyte-macrophage colony stimulating factor (GM-CSF). AV-GBM-1 consisted of autologous DC incubated with autologous tumor antigens contained in the lysate of irradiated cultured GBM cells. After recovery from RT/TMZ, doses were admixed with 500 mcg GM-CSF; up to 8 doses were injected subcutaneously over 6 months. Patients were not excluded by apparent progression or pseudo-progression post RT/TMZ. OS and progression-free-survival (PFS) were calculated from ITT enrollment. The success rate was 97% for both GBM cell cultures and collection of monocytes; 60/60 vaccines were successfully manufactured. Median age was 59 years. 57 patients received 392 injections. After two weekly injections there were significant increases in plasma lipocalin-2 and angiopoietin-1, and decreases in thrombospondin-5, angiotensinogen, and beta-fibroblast growth factor. The most common adverse events attributed to AV-GBM-1 were local injection site reactions (16%) and flu-like symptoms (10%). With follow up from 15.2 to 32 months, median PFS and OS were 10.3 (8.5,11.6 95% CI) and 16.0 (13.0,21.3 95% CI) months respectively. OS was better in the 25 patients who had *methylguanine-methyltransferase (MGMT)* methylation and/or *isocitrate dehydrogenase (IDH)* mutation. Age was not independently correlated with survival. From date of first injection, OS was not increased in 14 patients who were treated with alternating electrical tumor-treating fields. CONCLUSION: feasibility, safety, and PFS were encouraging. A phase III trial is in development.

Clinicaltrials.gov NCT03400917.

CLINICAL TRIALS: NON-IMMUNOLOGIC

CTNI-01. A PHASE 1-2 CLINICAL TRIAL OF EO1001 (APL-122), A NOVEL IRREVERSIBLE PAN-ERBB INHIBITOR WITH PROMISING BRAIN PENETRATION

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CNS metastases are a prominent driver of cancer morbidity and mortality, especially as targeted therapies have improved systemic outcomes. Mutations in the ErbB/HER kinase family are known oncodrivers in many cancers. Extensive crosstalk among ErbB/HER receptors suggests that inhibition of multiple family members may benefit treatment and limit drug resistance. There is a desperate need for new agents that are more tolerable and effective in treating CNS metastases. EO1001 (APL-122) is a first-in-class, oral, irreversible pan-ErbB inhibitor targeting ErbB1, ErbB2 and ErbB4 with promising CNS penetration in preclinical models. Preclinical data suggests a favorable pharmacokinetic and safety profile and activity against ErbB-driven cancers in patient-derived xenograft models. We report on a first-in-human Phase 1-2 clinical trial in progress. Adult participants with confirmed ErbB-positive cancer, including patients with CNS involvement, who have progressed after standard-of-care, with adequate bone marrow, renal and liver function are eligible. ESCALATION: One subject per dose cohort is enrolled in an accelerated dose-escalation design until drug-related toxicity (≥G2) is observed in the first cycle, after which dose escalation will revert to a 3 + 3 design to determine the maximum tolerated dose (MTD). *Cycle 1:* Patients receive a single oral dose of EO1001 on day 1; single-dose pharmacokinetics are measured. Beginning on day 8, EO1001 is administered once daily for 21 days; multi-dose pharmacokinetics are measured. *Cycles 2-6:* EO1001 is administered once daily in continuous 28-day cycles for up to 20 weeks. EXPANSION: EO1001 will be administered once daily to 20 patients at the MTD in continuous 28-day cycles for up to 6 cycles to determine a recommended Phase 2 dose (RP2D) for further study. Toxicity is assessed based on NCI CTCAEv5 and tumor response is assessed by RECIST 1.1. CNS exposure is evaluated in patients via CSF collection with confirmed CNS disease involvement.

CTNI-02. NERATINIB FOR TREATMENT OF LEPTOMENINGEAL METASTASES FROM HER2-POSITIVE BREAST CANCER IN EXTENDED ACCESS PROGRAM: PRELIMINARY RESULTS

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INTRODUCTION: The aim of the study was to evaluate the activity of neratinib in LM from HER2-positive BC after the failure of multiple lines of treatment. PATIENTS AND METHODS: Inclusion criteria were as follows: age ≥ 18 years; histological diagnosis of primary HER2-positive BC; newly-diagnosed LM (LANO criteria); KPS ≥ 60; coexistence of BM that have or not received radiotherapy; life expectancy ≥ 3 months; previous drugs, including capecitabine, trastuzumab, T-DM1, pertuzumab, and hormone therapy, were allowed, with the exclusion of lapatinib or other investigational agents. Neratinib was administered 240 mg daily continuously. Primary endpoint was the OS. Secondary endpoints were progression-free survival (PFS), neurological benefit, radiological response rate, and tolerability. RESULTS: Nine patients with LM have been enrolled with a median age of 44 years, and a median KPS of 80. Median time since LM onset from the diagnosis of primary BC was 42 months, and patients underwent a median number of adjuvant treatments before LM of 3. Three patients developed LM alone, and other 6 had LM associated with multiple BM. Six-months and 1-year OS were 66.7% and 22.3%, respectively, with a median OS of 8 months (95%CI 3-13*). Median PFS was 3.5 months (95%CI 2-6) after the start of treatment. A neurological improvement was reported in 2/9 patients (22.2%), while in other 4/9 patients (44.5%) was achieved a neurological stabilization lasting for a median time of 5 months (95%CI 2-19). The best radiological response was a stable disease in 5/9 patients (55.6%), while no complete or partial were achieved according to LANO criteria. A CSF clearance was observed in 1 patient only (11.1%). Grade III-IV adverse events were not reported, and 2 patients only (22.2%) had mild diarrhea correlated with neratinib. CONCLUSIONS: Neratinib might be a safe and effective treatment in LM from heavily pretreated HER2-positive BC.

CTNI-03. EXTENDED BENEFITS IN PATIENTS WITH RECURRENT HIGH GRADE GLIOMA THAT CONTINUOUSLY RECEIVE TOCA FC AFTER TOCA 511 TREATMEN

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Toca 511 (vocimagene amiretrorepvec) is an investigational nonlytic, retroviral replicating vector (RRV) constructed with a codon-optimized yeast cytosine deaminase (CD) gene. Toca 511 infects cancer cells, and stably delivers CD gene whose protein product converts courses of the prodrug TocaFC (5-fluorocytosine) into 5-fluorouracil (5-FU). Several phase 1 studies