mutant IDH1 peptide vaccine alone and in combination with temozolomide (TMZ). In the phase I RESIST clinical trial (NCT02193347), 34 patients were enrolled who had recurrent and resectable IDH1 R132H mutant grade 2 glioma received peptide vaccinations composed of 500 μg of mutant IDH1 peptide and 150 μg of GM-CSF mixed 1:1 with Montanide adjuvant prior to surgical resection. Vaccines 1, 2, and 3 were given 15 (+/-) 3 days apart. 7–12 days after vaccine 3, patients underwent standard of care tumor (SOC) resection. After resection, 23 patients had grade 2 gliomas and 11 patients with grade 3 gliomas were given up to 15 doses of peptide vaccine in combination with SOC therapy regimens while patients with transformed grade 3 gliomas were given up to 15 doses of peptide vaccine in combination with SOC therapy and TMZ regimens. T cell responses against the mutant peptide were measured after vaccine 3 using IFN-γ ELISPOT and intracellular flow cytometry for IFN-γ, TNFα, and IFNy. RESULTS: 3/20 patients were taken off the study before completion of study related activities. 1/20 patients progressed before completion of all vaccines. Out of 134 total doses of vaccine delivered, only one dose generated a grade 2 or higher injection-related toxicity according to the CTCAE guidelines. Vaccination with the mutant peptide led to an overall increase in IFN-γ spot-forming splenocytes specific to the mutant peptide (p=0.0408). CONCLUSION: Administering the mutant IDH1 peptide vaccine in patients with recurrent IDH-mutant gliomas was able to induce anti-IDH1 R132H immune responses in this initial phase I study.

IMMU-07. A PHASE I STUDY OF MULTIPLE PEPTIDE TUMOR-ASSOCIATED ANTIGEN VACCINES IN NEWLY DIAGNOSED Glioblastoma

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INTRODUCTION: Targeting tumor-associated antigens (TAAs) via peptide vaccine has been tested against malignant glioma with minimal success. Poor responses are attributed to relatively low antigen level expression or insufficient CD8+ T cell responses. Including a universal class II epitope that provides CD4+ T cell help towards CD8+ responses has been tested with the immunogenic tetanus toxoid epitope P30, but P30 has been employed as a separate peptide in this regard. The current study will employ targeting of three major glioma TAAs: EphA2, pp65 from Cytomegalovirus, and survivin. The ability to induce more potent TAA-specific immune responses will be tested using two novel strategies: P30-linked TAA peptides and a combinatorial vaccination of the linked peptides (P30-EPs).

HYPOTHESES: In Evaluation of Tumor Associated P30-Peptide Antigen I (ETAPA-I), P30-EPs is anticipated to have an acceptable toxicity profile. Multi-peptide vaccination is thought to bypass tumor heterogeneity and selection of antigen-negative clones, known as antigen escape. Moreover, the administration of EPS covalently linked to P30 is anticipated to increase the magnitude of antigen-specific immune responses and elicit both CD4- and CD8-mediated immune recognition. DESIGN/OBJECTIVES: A maximum of 24 patients with newly diagnosed, unmethylated WHO grade IV glioma will be treated. Following resection and standard of care immunomodulation, patients will be vaccinated serially during the priming phase (Day 1-22) and booster phase (Day 84 and 140). All P30-EPs vaccines during priming and boosting phases are co-administered with the adjuvant HN300 (Oncovec, poly-ICLC), and patients self-administer HN300 throughout the 96 week phase. The primary end point will evaluate safety profile of P30-EPs. Secondary objectives include polyfunctional T-cell responses specific to EphA2, pp65 and survivin, TCR diversity, and survival.

CONCLUSION: We describe a study that employs known TAA targets of malignant glioma with the novel strategy of combinatorial class I-linked peptide vaccination.

IMMU-08. PHASE II TRIAL OF PEMBROLIZUMAB AND LENVATINIB FOR LEPTOMENINGEAL METASTASES

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Leptomeningeal metastasis (LMD) is a late complication of cancer with poor prognosis and median survival of approximately 4–6 weeks without treatment. Whole brain radiation remains the mainstay of treatment, however it can cause significant neurocognitive sequelae and has not been shown to prolong overall survival. Thus, new treatment strategies are urgently needed to improve outcomes in patients with LMD. Results from recent Phase 2 studies of immune checkpoint inhibitors in LMD shows promising improvement in overall survival. Combining anti-VEGF therapy and immunomodulation may control symptoms due to inflammation and tumor-induced irritation, minimize steroid use, and promote improved efficacy of immunotherapy through modulation of the tumor immune microenvironment. We designed a multi-institutional, single-arm Phase 2 study of pembrolizumab and lenvatinib in patients with leptomeningeal metastases from any solid tumor. The primary objective is to estimate the overall survival rate at 6 months (OS6). A Simon two-stage design with a total sample size of 19 evaluable patients will be used to compare a null hypothesis of OS6 of 25% against an alternative hypothesis of 55%. Secondary objectives include assessing safety of pembrolizumab and lenvatinib in this patient population, systemic d50 of pembrolizumab and lenvatinib, estimating overall response rate, and progression-free survival. We will also explore clinician-reported neurologic outcomes and patient-reported quality of life and symptom burden. Blood, cerebrospinal fluid, and tissue biomarkers will be analyzed to determine predictors of 2-gliomas that are noted to have minimal doses of steroids prior to study enrollment and cannot have received prior immune checkpoint inhibitor or anti-VEGF therapy. Response to treatment will be determined using RANO-BM for intracranial disease and RECIST 1.1 for systemic disease. Study accrual is anticipated over 12-24 months with anticipated total study duration of 30 months.

FINAL CATEGORY: NEUROIMAGING

NEIM-01. PREDICTION OF RESPONSE TO COMBINATION OF NIVOLUMAB AND BEVACIZUMAB IN PATIENTS WITH RECURRENT Glioblastoma via Radiomic Analysis on Clinical MRI Scans

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PURPOSE: The use of immunotherapy in glioblastoma management is under active investigation. Glioblastomas are “cold” tumors, meaning that they have inactivated or fewer tumor infiltrative lymphocytes in addition to substantial tumor necrosis, attributing to their poor response to immunotherapy. A significant challenge is the apriori identification of Glioblastoma patients who will respond favorably to immunotherapy. In this work, we evaluated the ability of computerized MRI-based quantitative features (radiomics) extracted from the lesion habitat (including enhancing lesion, necrosis, and peritumoral hyperintensities) to predict response and progression-free survival (PFS) in recurrent GBM patients treated with combination of Nivolumab and Bevacizumab. METHODS: Immunotherapy response assessment in neuro-oncology (iRANO) criteria along with PFS were used to analyze n=50 patients enrolled in a randomized clinical trial where patients received Nivolumab with either standard or low dose Bevacizumab. These patients were assessed to see if they had complete response, partial response, stable disease (i.e. responders, n=31), or disease progression (i.e. non-responders, n=19). Lesion habitat constituting necrotic core, enhancing tumor, and edema were delineated by expert radiologist on Gd-T1w, T2w and FLAIR MRI scans. COLAGE radiomic features from each of the delineated regions were selected using minimum redundancy maximum relevance (mRMR) via cross-validation, to segregate non-responder patients from responders. A multivariable Cox proportional hazard model was used to predict survival (PFS). RESULTS: Using COLAGE correlation, sum average, and sum variance features (capture local heterogeneity) from the lesion habitat, we found to segregate non-respondent patients from responders with an accuracy of 86%, followed by 80% using features from peritumoral hyperintensities and 78% from enhancing tumor. CONCLUSION: In this work, we evaluated the ability of computerized MRI-based quantitative features (radiomics) extracted from the lesion habitat (including enhancing lesion, necrosis, and peritumoral hyperintensities) to predict response and progression-free survival (PFS) in recurrent GBM patients treated with combination of Nivolumab and Bevacizumab.

NEIM-02. TRIAL IN PROGRESS: A MULTICENTER PHASE 3 STUDY TO ESTABLISH THE DIAGNOSTIC PERFORMANCE OF 18F-FLUCILIVONE PET IN DETECTING RECURRENT BRAIN METASTASES AFTER RADIATION THERAPY (REVEAL)

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BACKGROUND: Brain metastases occur in up to 40% of patients with cancer and are associated with poor prognosis and considerable levels of recurrence. Consequently, close follow-up with serial brain MRI is performed post-treatment to detect early disease. Although conventional MRI (CE-T1-weighted and FLAIR/T2-weighted) is the recommended follow-up modality, it has poor specificity with limited ability to differentiate between true disease recurrence and treatment-related changes such as radiation necrosis. Therefore, alternative imaging options are sought in order to improve patient outcomes. METHODS: A multicenter, prospective, randomized, phase 3 trial, with two co-primary objectives will be used to compare the performance of 18F-FLUCILIVONE PET/CT to conventional imaging for detection of radiographic evidence of recurrence during follow-up after initial radiation therapy. Patients are eligible if they have at least one measurable brain metastasis on baseline imaging (MRI or contrast enhanced CT) with lead radiotracer uptake. Inclusion criteria includes patients aged 18 to 75 years with histologically confirmed brain metastasis from any solid tumor. The primary endpoint is to estimate the overall response rate at 12 months. A Simon two-stage design with a total sample size of 50 evaluable patients will be used to compare a null hypothesis of ORR of 25% against an alternative hypothesis of 65%. Secondary objectives include assessing safety of 18F-FLUCILIVONE PET/CT within the 30-day window prior to and 30 days post the administration of 18F-FLUCILIVONE for large radiotracer uptake. The study design is a prospective, randomized, open-label, two-arm, single-center trial. The trial is registered with ClinicalTrials.gov (NCT03632008).