Title

CTNI-53. RADIATION TREATMENT VOLUMES BEFORE AND AFTER BRAF/MEK THERAPY IN NEWLY DIAGNOSED PAPILLARY CRANIOPHARYNGIOMAS: A CORRELATIVE ANALYSIS OF THE ALLIANCE A071601 PHASE II TRIAL

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CTNI-52. RETROSPECTIVE ANALYSIS OF USING RADIOTHERAPY WITH CONCURRENT TEMOZOLOMIDE AND TUMOR TREATING FIELDS FOR CHINESE PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA

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OBJECTIVES: Tumor Treating Fields (TTFields) has been shown to improve the overall survival of newly diagnosed GBM (ndGBM) when combined with Temozolomide (TMZ) in the EF-14 trial. Preclinical studies suggested synergistic effects between TTFields and radiotherapy. This study is aimed to examine the safety and efficacy of combination therapy (chemoradiation concurrent with TTFields treatment) for ndGBM patients in China. METHODS: From July 2020 to May 2021, 33 ndGBM patients were treated with combination therapy (radiation target volume following NCCN guidelines). Eight patients had transducer array removed during radiotherapy, others retained transducer array on scalp. All patients had assessment every two months by MRI scan. The adverse reactions and monthly compliance data for TTFields treatment were recorded. RESULTS: Twenty-five patients have completed the combination therapy. Three patients retained transducer array during radiotherapy but did not limit the scalp dose (mean: 21.7Gy). As a result, Grade 2 cutaneous adverse reactions developed, and TTFields treatment was suspended. Four patients suspended TTFields treatment due to other adverse reactions. The remaining patients who had limited scalp doses (mean < 20Gy) had no suspension or delay in combination therapy due to cutaneous adverse reactions. The median time of TTFields treatment during radiotherapy is 21.24 hours/day (IQR:19.26,22.08). Two patients had progressive disease, 1 died of pulmonary infection, and 30 had stable disease. The incidence of cutaneous AE was 48.5% (16/33), Grade1: 27.2% (9/33), Grade 2: 21.2% (7/33), and Grade 3: 3% (1/33). CONCLUSIONS: The combination therapy was well tolerated in Chinese patients with ndGBM. Removing transducer array during radiotherapy may increase the frequency of array replacement while reducing the patient's daily treatment time. However, retaining transducer array will increase cutaneous adverse reactions. Scalp dose limitation is required yet it allows a maximum duration of TTFields. Further follow-ups are ongoing.

CTNI-53. RADIATION TREATMENT VOLUMES BEFORE AND AFTER BRAF/MEK THERAPY IN NEWLY DIAGNOSED PAPILLARY CRANIOPHARYNGIOMAS: A CORRELATIVE ANALYSIS OF THE ALLIANCE A071601 PHASE II TRIAL

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PURPOSE: Standard of care for craniopharyngiomas is surgery with or without radiotherapy (RT). Cohort A of Alliance A071601 evaluated the efficacy of BRAF/MEK inhibition with vemurafenib/cobimetinib in patients with previously untreated papillary craniopharyngiomas (PCP), which carry the *BRAF V600E* mutation. Cohort B is currently enrolling patients with recurrence after RT. In a correlative analysis, we examined changes in RT volumes after BRAF/MEK therapy in Cohort A. METHODS: Previously unirradiated patients with BRAF-mutated PCP were treated with vemurafenib/cobimetinib. Sixteen patients had scans available before starting vemurafenib/cobimetinib ("pre-therapy") and after completing therapy ("post-therapy"). Two patients went off study treatment after 8 and 9 days due to side-effects and were excluded for this analysis. Gross target volumes (GTV) were contoured on pre-therapy and post-therapy scans. On post-therapy scans, an additional target comprising gross disease and at-risk regions for microscopic residual disease (GTV-micro) was defined and considered the treatment volume. Clinical target volume (CTV) was a 5-mm uniform expansion on pre-therapy GTV and post-therapy GTV-micro. Volumes were independently reviewed by two radiation oncologists. Changes in volumes from pre- versus post-therapy were compared using the Wilcoxon signed rank test. RESULTS: In 14 patients evaluated, 57% were female and median age at enrollment was 49.5 years (range 33-83). Median time on treatment was 8.9 months (range 4.0-18.0). Median GTV pre-therapy was 3.8 mL (range 0.2-23.4) versus 0.3 mL (range 0.0-3.2) post-therapy (p=0.0001) and 1.7 mL (range 0.1-8.0) post-therapy GTV-micro (p=0.0001). Median CTV pre-therapy was 13.7 mL (range 2.8-51.8) versus 9.1 mL (range 2.2-27.5) post-therapy (p=0.0001). All tumors abutted the optic chiasm pre-therapy, only 6 did post-therapy. CONCLUSIONS: Vemurafenib/cobimetinib resulted in smaller RT volumes. BRAF/MEK inhibitors could reduce RT volumes and spare dose to surrounding normal structures. Enrollment to Cohort B of Alliance A071601 should be considered for patients with recurrent tumors after RT. SUPPORT: https://acknowledgments.alliancefound.org

CTNI-54. A SINGLE ARM PHASE II STUDY OF THE DUAL MTORC1/MTORC2 INHIBITOR VISTUSERTIB PROVIDED FOR SPORADIC PATIENTS WITH GRADE II-III MENINGIOMAS THAT RECUR OR PROGRESS AFTER SURGERY AND RADIATION

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Grade II/III meningiomas have increased rates of recurrence with no approved medical therapies. The historical progression-free survival at 6 months (PFS-6) is 25% with rates >35% declared of interest for drug development. *NF2* gene inactivation occurs in about half of meningiomas. Based on our studies showing mTORC1 and mTORC2/SGK1 pathway activation in *NF2*-deficient meningiomas and the paradoxical activation of the mTORC2/AKT pathway, we hypothesized that mTORC1/mTORC2 inhibitors would be active in meningiomas. We studied the effect of vistusertib in patients with progressive/recurrent grade II/III meningiomas (NCT03071874). Vistusertib was administered orally at 125mg twice daily on two consecutive days each week. MRIs were obtained every 56 days. Tumor size was defined as the largest cross-sectional area. Progression was defined as ≥ 25% increase in the sum of products of all measurable lesions over smallest sum observed. The primary endpoint was PFS-6. Secondary endpoints included toxicity, radiographic response, and correlative studies including immunohistochemistry for mTORC1/2 pathway activation and genetic biomarkers. Twenty-eight patients (13 female, median age 58 years, median KPS 80%) were enrolled. Median tumor size was 4.4cm; 71% were grade II and 50% harbored pathogenic *NF2* variants. Four patients discontinued treatment voluntarily and 1 each withdrew for intercurrent illness and non-compliance. PFS-6 is 47% (CI, 26%-65%) and OS-12 is 72% (95%CI, 48%-86%). PFS but not OS was shorter for patients with grade 3 meningiomas; there was no difference in PFS/OS between genetic groups. Adverse events at least possibly related to vistusertib with frequency >10% include nausea, fatigue, hypophosphatemia, diarrhea, anorexia, dry mouth, hypertriglyceridemia, hypertension, vomiting, increased ALT, constipation, and weight loss. Vistusertib treatment was associated with a PFS-6 rate exceeding the target of 35% for recurrent high-grade meningioma. Adverse events were tolerable in this patient population. These data support the continued development of mTORC1/2 inhibitors in this setting.

CTNI-55. THE CDK4/6 INHIBITOR ABEMACICLIB IN PATIENTS WITH RECURRENT MENINGIOMA AND OTHER PRIMARY CNS TUMORS

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BACKGROUND: Medical therapies for recurrent brain tumors are limited. Abemaciclib is a small molecule CDK4/6 inhibitor that has demonstrated antitumor activity in multiple cancer types and crosses the blood-brain barrier. METHODS: We conducted a phase II trial of single-agent abemaciclib in patients with recurrent primary brain tumors utilizing a novel CNS basket trial design with multiple tumor types accrued to separate cohorts including patients with recurrent IDH-wildtype gliomas (Cohort A), any recurrent gliomas requiring cytoreductive surgery (Cohort