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Abstract

LATE BREAKING

LTBK-01. INO-5401 AND INO-9012 DELIVERED INTRAMUSCULARLY (IM) WITH ELECTROPORATION (EP) IN COMBINATION WITH CEMIPLIMAB (REGN2810) IN NEWLY DIAGNOSED GLIOBLASTOMA

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BACKGROUND: Novel T cell-enabling therapies, in combination with checkpoint inhibition, may improve OS in GBM. INO-5401 (synthetic DNA plasmids encoding hTERT, WT-1, PSMA) plus INO-9012 (synthetic DNA plasmid encoding IL-12), and the PD-1 immune checkpoint inhibitor cemiplimab, is given to patients with newly diagnosed GBM to evaluate tolerability, efficacy and immunogenicity. **METHODS:** Phase I/II, single arm, 2 cohort study (A: MGMT unmethylated, B: MGMT methylated). Primary endpoint is safety; efficacy and immunogenicity are secondary. Nine mg INO-5401 plus 1 mg INO-9012 (every 3 weeks x 4 doses, then Q9W) is given IM with EP by CELLECTRA® 2000 with cemiplimab (350 mg IV Q3W). RT is given as 40 Gy over 3 weeks. TMZ is given with radiation (all patients), and adjuvantly (Cohort B only). RESULTS: Fifty-two subjects enrolled: 32 in Cohort A; 20 in Cohort B. 35% women; median age 60 years (19–78 years). The adverse event profile is consistent with single-agent (INO-5401, INO-9012, EP and cemiplimab) reported events. OS at 12 months was 84.4% (Cohort A) and 85% (Cohort B). OS at 18 months in Cohort A is 50% (95% CI 31.9 - 68.1); median OS is 17.9 months (14.5 - NR); Cohort B OS18 and median OS will be presented. Tumor gene transcripts at diagnosis confirmed expression of INO-5401 antigens. Peripheral immune responses following INO-5401 revealed antigen-specific T cell responses by Interferon gamma ELISpot and flow cytometry, including cytokine production and expansion of antigen specific CD8+T cells with lytic potential. CONCLUSIONS: INO-5401 + INO-9012, a novel DNA plasmid immunotherapy, demonstrates acceptable risk/benefit and generates robust systemic immune responses to encoded tumor antigens when administered with cemiplimab and RT/TMZ in newly diagnosed GBM patients. Overall survival is encouraging. Clinical trial information: NCT03491683.

LTBK-04. PHASE 2 MULTICENTER STUDY OF THE ONCOLYTIC ADENOVIRUS DNX-2401 (TASADENOTUREV) IN COMBINATION WITH PEMBROLIZUMAB FOR RECURRENT GLIOBLASTOMA; CAPTIVE STUDY (KEYNOTE-192)

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BACKGROUND: A Phase 2 multi-center study was conducted to evaluate the replication-competent oncolytic adenovirus, DNX-2401 (tasadenoturev), in combination with the anti-PD-1 antibody, pembrolizumab, in subjects with recurrent glioblastoma. METHODS: Subjects ≥ 18 years with glioblastoma at first or second recurrence were treated with a single intratumoral injection of 5e8-5e10 vp DNX-2401 at the time of biopsy, followed by 200 mg pembrolizumab infusions every 3 weeks until progression or toxicity. RESULTS: Forty-nine subjects were enrolled at first (79.6%) or second (20.4%) recurrence after prior surgery (89.8%), radiotherapy (100%), and temozolomide (100%). Forty-eight of 49 (98%) were treated with 5e8 vp (n=3), 5e9 vp (n=3), or 5e10 vp (n=42) DNX-2401 and pembrolizumab. Median treatment duration was 7 cycles (range 1–35) with one subject remaining on treatment (cycle 31). Adverse events were primarily mild to moderate, consistent with underlying disease, and manageable. Headache, brain edema, and fatigue are the most common events reported as related to the treatment regimen. Of subjects treated with full dose DNX-2401 and pembrolizumab (n=42), 5 subjects (11.9%) had confirmed responses, including 2 durable ongoing complete responses and 3 partial responses. One subject remains tumor free > 12 months after completing the planned 24 months of pembrolizumab. Median overall survival was 12.5 months; OS-12 and OS-18 were 54.5% and 20.8%, respectively. Four subjects, all of which have survived more than 21 months, continue to be followed for survival. CONCLUSIONS: DNX-2401 plus pembrolizumab provides encouraging activity and is safe in patients with recurrent glioblastoma. A global, randomized, controlled Phase 3 study is planned.