DNX-2401

A phase I, dose-escalation, biologic-end-point clinical trial of DNX-2401 was conducted in 37 patients with recurrent malignant glioma. Patients received a single intratumoral injection of DNX-2401 into biopsy-confirmed recurrent tumor to evaluate safety and response across eight dose levels (group A). To investigate the mechanism of action, a second group of patients (group B) underwent intratumoral injection through a permanently implanted catheter, followed 14 days later by en bloc resection to acquire post-treatment specimens. Results In group A (n = 25), 20% of patients survived > 3 years from treatment, and three patients had a ≥ 95% reduction in the enhancing tumor (12%), with all three of these dramatic responses resulting in > 3 years of progression-free survival from the time of treatment. Analyses of post-treatment surgical specimens (group B, n = 12) showed that DNX-2401 replicates and spreads within the tumor, documenting direct virus-induced oncolysis in patients. In addition to radiographic signs of inflammation, histopathologic examination of immune markers in post-treatment specimens showed tumor infiltration by CD8+ and T-bet+ cells, and transmembrane immunoglobulin mucin-3 downregulation after treatment. Analyses of patient-derived cell lines for damage-associated molecular patterns revealed induction of immunogenic cell death in tumor cells after DNX-2401 administration. Conclusion Treatment with DNX-2401 resulted in dramatic responses with long-term survival in recurrent high-grade gliomas that are probably due to direct oncolytic effects of the virus followed by elicitation of an immune-mediated antiglioma response [1].

In a Phase I, single-center, uncontrolled trial. A tumor biopsy will be performed through the cerebellar peduncle, and DNX-2401 will be injected immediately after the biopsy. Standard therapy consisting of radiotherapy and chemotherapy will follow in 2 to 6 wk.

EXPECTED OUTCOMES: Improvement of overall survival and quality of life in patients with DIPG and collection of tumor specimens to study the molecular profiling of these tumors.

The aims of this trial are to contribute to the sample collection of DIPG and to offer treatment during the tumor tissue biopsy using the virus. If this virus works as expected, it could kill the tumor cells with no damage to healthy tissue, functioning as a targeted therapy. It is important to note that edema has not been observed with this virus in all trials performed to date. The information obtained through this and other similar studies may be useful for developing or improving new therapies in the battle against DIPG [2].

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2)
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