Results of Controlled IL-12 Monotherapy in Adults with Grade III or IV Gliomas

Background on Controllable IL-12

Methods

• Primary endpoint: Time to Progression (TTP) in subjects with unifocal disease
• Secondary endpoints: OS, PFS, RECIST response rates, IHC and Ki-67, laboratory marker and adipocytokine levels, safety

Study Design

• nCT02026273: Phase 1 trial (NCT02026273) is the first to evaluate the safety and tolerability of Ad-RTS-HL12 (Ad) under transcriptional control with veledimex (V) in adults with grade III or IV gliomas

Methods

• Multicenter, phase 1, open-label, 3 + 3 dose escalation study of Ad (single intratumoral injection, 2 × 10^{10} viral particles, Day 0) with oral V dosing (Days 0 to 14) of 10, 30, 40, and 60 mg in patients with glioblastoma multiforme (GBM) and anaplastic astrocytoma

Results

• 38 subjects were treated (treatment group: V 10 mg (n=6), 20 mg (n=15), 30 mg (n=4), 40 mg (n=6)), and 11 were evaluable (V 10 mg = 6, V 30 mg = 2, V 40 mg = 3).

Conclusions

• Results were promising, with V-dependent and proportional increase in cytokine concentrations (INF- gamma, IL-12p70) during active dosing (Days 0-14) and on-treatment immune biomarker profiles

Safety Results:

- No dose-limiting toxicities
- Grade 3 adverse events:
  - Neutropenia
  - Leukopenia
  - Headache
  - Meningitis
  - Nausea
- Grade 4 adverse events:
  - Seizure
  - Cerebral haemorrhage
  - Hyponatraemia

Pharmacokinetic and Exposure Response With Increased Veledimex Dose

There is a dose-dependent increase of veledimex concentrations in cerebrospinal fluid (CSF), tumor tissue, and plasma samples from subjects treated with veledimex among different dose cohorts

Discussion and Conclusions

• Results of Controlled IL-12 in GBM are promising, with V-dependent and proportional increases in IL-12 and IFN-γ resulting in immune activation, with a safety profile and encouraging survival. The 20 mg dose is the recommended phase 2 dose. Controlled IL-12 is being evaluated in a phase 2 study in pediatric subjects (NCT03330197) and as a monotherapy in adults with GBM (NCT02026273).