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**CORE1: PHASE 2, SINGLE ARM STUDY OF CG0070  
COMBINED WITH PEMBROLIZUMAB IN PATIENTS WITH  
NON MUSCLE INVASIVE BLADDER CANCER (NMIBC)  
UNRESPONSIVE TO BACILLUS CALMETTE-GUERIN (BCG)**

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**Background** CG0070, an oncolytic vaccine available as an intravesical therapy, is a serotype 5 adenovirus engineered to express GM-CSF and replicate in tumor cells with mutated or deficient RB (which results in increased of the transcription factor E2F). The CG0070 mechanism of action includes direct cell lysis in conjunction with immunogenic cell death which is enhanced in the presence of GM-CSF. In an initial phase 1 study as well as a subsequent phase 2 study, an overall CR rate of ~62% and a CR at 12 months (m) of 29% have been observed in patients with high risk NMIBC previously treated with BCG. Intravenous Pembrolizumab was recently approved by the FDA for patients with BCG-unresponsive CIS (with or without papillary tumors) with an overall complete RR of 41% and a 12m CR rate of ~20%. This phase 2 study (NCT04387461) will assess the potential synergy of the two agents in the treatment of BCG-unresponsive NMIBC.

**Methods** 35 patients with BCG-unresponsive CIS with or without concurrent Ta or T1 disease will be treated with intravesical (IVE) CG0070 at a dose of 1x10<sup>12</sup> vp in combination with pembrolizumab at a dose of 400 mg IV q6 weeks. CG0070 will be administered weekly x 6 as induction followed by weekly x 3 maintenance instillations at 3, 6, 9, 12, and 18m. Patients with persistent CIS or HG Ta at 3 m may receive re-induction with weekly x 6 CG0070. Pembrolizumab will be administered up to 24m. Assessment of response will include q 3m cystoscopy with biopsy, urine cytology, CTU/MRU, and mandatory bladder mapping biopsies at 12m.

**Results** The primary endpoint is CR at 12 m. Secondary endpoints will include CR at any time, progression free survival, duration of response, cystectomy free survival and the safety of the combination. Correlate assessments will include changes in the TME, systemic immune induction, viral replication and transgene expression. Baseline expression of PD-L1, coxsackie adenovirus receptor, E2F transcription factor as well as anti-adenovirus antibody titer will be correlated with tumor response. At this time the first 5 patients demonstrates 100% 3 m CR. Treatment related AE have been limited to transient grade 1-2 urinary frequency (3 patients) and grade 1 bladder spasm, hematuria, painful urination, thyroiditis, and flu-like symptoms (one patient/each). No grade 3, 4, 5 AE or SAE were observed.

**Conclusions** The study is currently enrolling. Preliminary safety and efficacy data on 8 patients will be available by November 2021

**Trial Registration** NCT04387461

**Ethics Approval** IRB: CG2003C

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