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)

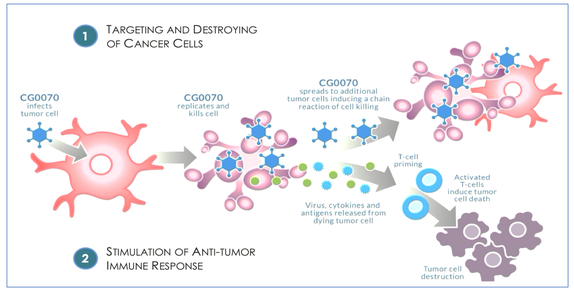
Roger Li[1], Gary D. Steinberg [2] , D. Lamm[3], E. Uchio[4], Paras Shah[5], Ashish Kamat[6], Trinity Bivalacqua[7], Michael Chisamore[8], Nataliya Hnat[9] , John McAdory [9], Paola Grandi[9], James Burke,[9]

[1]Moffitt Cancer Center, Tampa, FL; [2]NYU Langone Health, New York, NY, [3]Atlantic University of Arizona College of Medicine, Phoenix, AZ; [4]The University of California, Irvine, CA; [5]Mayo Clinic, Rochester, MN ; [6]University of Texas MD Anderson Cancer Center, Houston, TX; [7] University of Pennsylvania, Philadelphia, PA; [8] Merck & Co. Inc, Rahway, NJ, USA, [9]CG Oncology, Inc. 400 Spectrum Center Drive, Suite 2040, Irvine, CA

Overview

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 free levels of the transcription factor E2F). The CG0070 mechanism of action includes direct cell lysis in conjunction with immune mediated cell death which is enhanced in the presence of GM-CSF. In an initial phase 1 study as well as a subsequent open label 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, a PD-1 checkpoint inhibitor, 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 12 m 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

Oncolytic Immunotherapy



(1) Tumor-selective infection and replication of the virus, followed by cell killing, inducing local inflammation and trafficking of immune cells to the infected tumor site (2) priming and amplification of systemic antitumor immunity, resulting in Induction of tumor-antigen-specific T cells that can eliminate uninfected tumor cells, including distant metastases

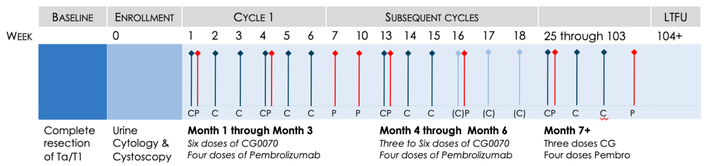
CG0070

In CG0070, the human E2F-1 promoter drives expression of the essential viral genes and restricts viral replication to retinoblastoma (Rib) gene pathway defective tumor cells, selectively killing these cells with minimal damage to normal tissues. In addition, CG0070 encodes the cDNA for human GM-CSF expressed and secreted by tumor cells transduced with CG0070.

E2F1	In Rib-pathway defective cells, Rb doesn't bind to E2F, leading to select replication of CG0070 in cancer cells
E1A	Essential viral gene
GM-CSF	Activator of Antigen Presenting Cells

Phase 2 Study for NMIBC (CORE1)

Study Administration Schedule:



- 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 $1x10^{12}$ up 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 months 3, 6, 9, 12, and 18.
- 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 pembrolizumab will be administered up to 18 cycles or approximately 24 m.
- Assessment of response will include q 3 m cystoscopy with biopsy of areas suspicious for disease, urine cytology, CTU/MRU, and mandatory bladder mapping biopsies at 12 m. Recurrence of HG disease will be enumerated as disease recurrence.

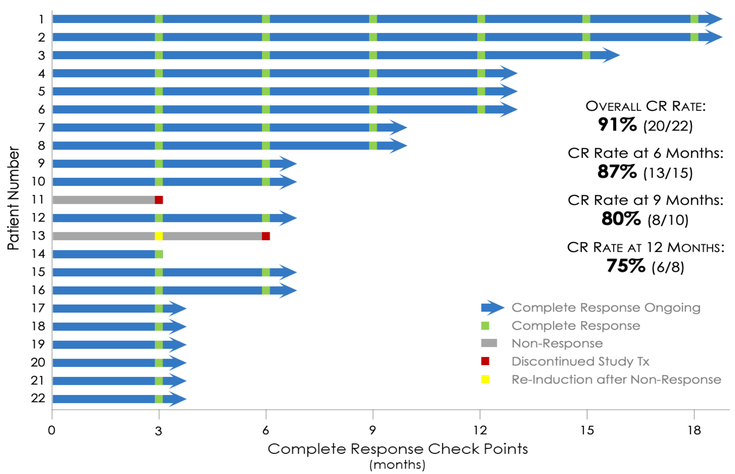
Key Objectives:

- The primary endpoint of the study 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.

RESULTS

EFFICACY

Duration of Response of Combination Therapy in BCG-Unresponsive



SAFETY

Preferred Term	Grade 1	Grade 2	Total
Pollakiuria	5	1	6
Bladder spasm	2	2	4
Dysuria	3	1	4
Fatigue	3	1	4
Nocturia	2	1	3
Chills	2		2
Haematuria	2		2
Micturition urgency	2		2
Polyuria	2		2
Arthralgia	1		1
Autoimmune thyroiditis	1		1
Blood thyroid stimulating hormone increased	1		1
Device leakage	1		1
Diarrhoea	1		1
Headache	1		1
Hot flush	1		1
Hyperglycaemia		1	1
Hypothyroidism		1	1
Influenza like illness	1		1
Joint stiffness	1		1
Malaise	1		1
Musculoskeletal stiffness	1		1
Myalgia	1		1
Penile haemorrhage	1		1
Pruritus		1	1
Pyrexia	1		1
Urinary tract infection		1	1
Urinary tract pain	1		1
Grand Total (Data cut-off 31Jan2022)	38	10	48

CONCLUSIONS

- The combination of CG0070 and pembrolizumab appears promising to date based on preliminary data showing efficacy beyond that observed in past studies for either agent alone in conjunction with a tolerable safety profile in line with the prior the adverse event profile reported for each agent as monotherapy. Complete enrollment with data readout on all patients through a minimum of 3 months is expected in the second half of 2022 with 12 month data on all patients anticipated in the first half of 2023 (NCT04387461).

This study was in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

CG Oncology