

CG0070, an Oncolytic Adenovirus, for BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer (NMIBC): 12 Month Interim Results and Biomarker Analysis from A Multicenter Phase II Trial

Introduction and Objectives: CG0070 is a selective oncolytic adenovirus that exploits retinoblastoma pathway defects. We previously showed promising 6 month response of intravesical CG0070, but longer term efficacy and response correlation with biomarker expression is unknown. We performed 12 month evaluation of a phase II trial for CG0070 in patients with BCG-unresponsive NMIBC who refused cystectomy.

Methods: Sixty-seven patients with residual BCG-unresponsive high grade Ta, T1, or CIS +/- Ta/T1 were accrued in this phase II single arm multicenter trial (NCT02365818). Patients recurred within 6 months of BCG induction (BCG-unresponsive) or developed subsequent recurrence (BCG-relapsing). CR was defined as no disease on cytology, cystoscopy, and random biopsies. Six patients were excluded for withdrawn consents due to inadequate drug availability or subsequent therapy despite CR prior to 12 months. Protein (pRb) and phosphorylated (ppRb) epithelial Rb expression, total PD-L1 expression, and CD8+ T-cell infiltration were scored and correlated with 6 month CR.

Results: At interim analysis of 61 patients, overall 12 month CR was 30% (Figure 1). CIS-containing tumors had 27% 12 month CR (n=45) while pure Ta/T1 had 38% (n=16). No patients with T1 + CIS/Ta had 12 month CR (n=6). BCG-unresponsive status was used to stratify 12 month CR: BCG-unresponsive was 48% (n=25), BCG-relapsing 19% (n=31), unknown 0% (n=5). Ten patients underwent cystectomy— 4 patients had muscle invasive disease. All 12 month treatment related adverse events (AEs) were Grade 1-3; immunologic AEs included influenza type illness (6%), fatigue (6%), and chills (3%). Three deaths were secondary to progressive urothelial carcinoma, esophageal carcinoma, and cardiac disease. There was significant heterogeneity of expression of pRb and ppRb. There was no correlation with 6 month CR and pRb, ppRb, PD-L1, or CD8+ levels.

Conclusion: Interim assessment of this phase II study demonstrates that intravesical CG0070 yielded an overall 30% complete response rate at 12 months for all patients with high-risk BCG-unresponsive NMIBC and 48% for those with BCG-refractory disease. There was no correlation with CR and evaluated biomarkers.

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