CG0070, an Oncolytic Adenovirus, for BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer (NMIBC): 18 Month Follow-Up from A Multicenter Phase II Trial

Introduction and Objectives: CG0070 is a selective oncolytic adenovirus that exploits retinoblastoma (Rb) pathway defects. We have previously shown promising interim results for this agent. We present mature results from 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 were unable to achieve disease free state at 6 months after adequate BCG (BCG-refractory) or developed recurrence after complete response (CR) to BCG (BCG-relapsed). CR was defined as no disease on cystoscopy, cytology, and/or random biopsies. The primary endpoint was 18-month CR. Ten patients were excluded from the analyses based on withdrawal of consent, or initiation of subsequent therapy despite continued CR prior to 18 months. One patient was excluded due to pending 18-month follow-up studies.

Results: On analysis of 56 patients, the overall 18-month CR rate was 21% (Figure 1), Among patient subsets, the 18-month CR rate was 17% (CIS-containing tumors, n = 42), 36% (pure Ta, T1 or Ta/T1, n=14). Based on response to prior BCG, 18-month CR rates were 32% (BCG-refractory, n=22), 17% (BCG-relapsed, n=29), and 0% (unknown, n=5). Eleven patients underwent cystectomy, of which 6 patients had muscle invasive disease. All treatment related adverse events (AEs) were Grade 1-3; immunologic AEs included influenza type illness (7%), fatigue (4%), and chills (1%). Six deaths were secondary to progressive urothelial carcinoma, esophageal carcinoma, lung carcinoma, and cardiac disease.

Conclusion: This phase II study demonstrates that in a high-risk BCG-unresponsive NMIBC population, intravesical CG0070 yielded overall 44%, 30%, and 21% complete response rates at 6, 12, and 18 months, respectively. Rb and checkpoint biomarker analysis is pending to attempt prediction of which patients have durable response to this agent.

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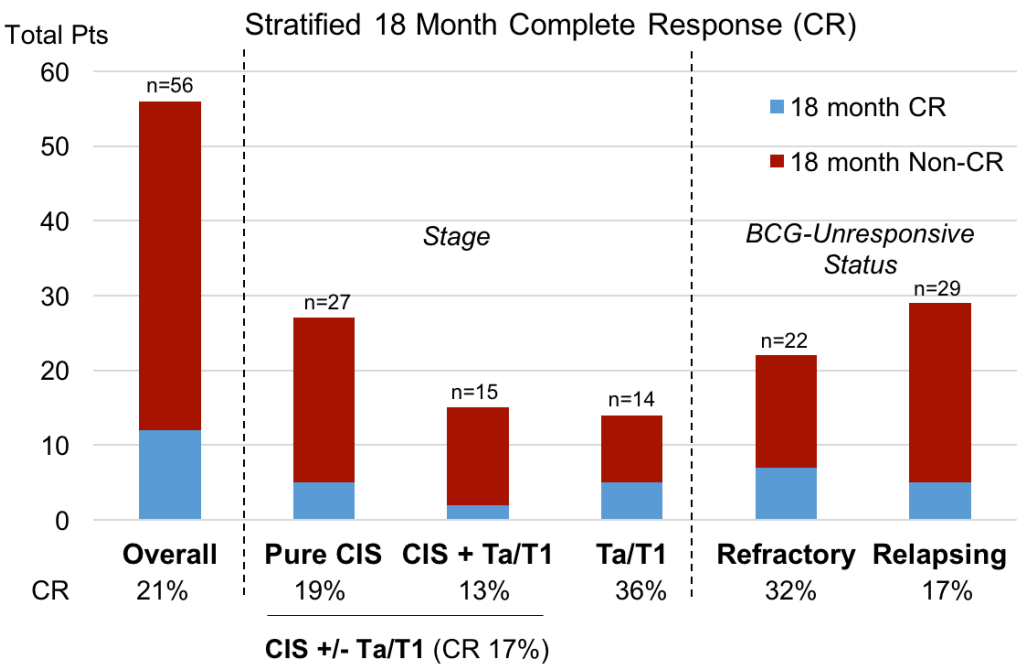
Stratified 18 Month Complete Response (CR)
Total Pts
60
50
40
30
20
10
0
n=56
n=27
n=15
n=14
n=22
n=29
18 month CR
18 month Non-CR
Stage
BCG-Unresponsive Status
Overall
Pure CIS
CIS + Ta/T1
Ta/T1
Refractory
Relapsing
CR
21%
19%
13%
36%
32%
17%
CIS +/- Ta/T1 (CR 17%)