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A Phase III Study to Evaluate the Safety and Efficacy of Intravesical Nadofaragene Firadenovec for Patients with High-Grade, BCG Unresponsive Non-Muscle Invasive Bladder Cancer: Papillary Disease Cohort Results

Stephen Boorjian, Rochester, MN, Colin Dinney, Houston, TX, The Society of Urologic Oncology Clinical Trials Consortium, Schaumburg, IL*

INTRODUCTION AND OBJECTIVE: A subset of patients (pts) with high-grade non-muscle invasive bladder cancer (NMIBC) who are treated with BCG will have BCG unresponsive disease, and are at considerable risk for tumor recurrence and progression. The development of effective intravesical therapies represents an important unmet need in this population. Nadofaragene firadenovec is a novel intravesical gene-mediated therapy that delivers the human IFN α 2b gene resulting in sustained IFN α 2b expression, and provided durable responses in a previous Phase 2 trial. Herein, we report results from the papillary disease (PD) cohort of the Phase 3 trial.

METHODS: This multicenter, open-label Phase 3 study investigated nadofaragene for high-grade NMIBC (carcinoma in situ [CIS \pm Ta/T1], or PD [Ta/T1 alone]) unresponsive to BCG. Nadofaragene (3×10^{11} vp/mL [75 mL]) was administered intravesically once every 3 months for up to 4 doses in the initial 12 months. Pts with no evidence of high-grade disease at month 12 were offered continued treatment at the investigator's discretion. The primary endpoint was complete response (CR) rate at any time in the CIS cohort (results presented in a prior abstract). Secondary end points included rate and durability of high-grade-recurrence-free (HGRF) survival as well as safety in PD pts, reported herein.

RESULTS: A total of 157 pts were enrolled, of whom 50 were in the PD cohort (safety population n=50; efficacy population n=48). At study entry, all pts were BCG-unresponsive. Of the 48 pts in the efficacy population, 35 (72.9%), 30 (62.5%), 28 (58.3%), and 21 (43.8%) achieved HGRF survival at months 3, 6, 9, and 12, respectively. Within this PD cohort, the most common treatment-emergent adverse events (TEAEs) were transient in nature; specifically, instillation site discharge 30%; bladder spasm 18%; micturition urgency 18%; urinary tract infection 18%. The most common drug-related TEAEs were instillation site discharge 26%; bladder spasm 14%; micturition urgency 14%; dysuria 14%. Grade 3 TEAEs were reported in 9 pts (3 study drug-related), with a single Grade 4 (not related to study drug). No pt had an adverse event leading to death.

CONCLUSIONS: Nadofaragene firadenovec was well tolerated and achieved an encouraging, durable HGRF survival in high-grade BCG-unresponsive NMIBC pts with PD. This demonstrates a clinically meaningful benefit in a pt population for whom to date non-surgical treatment options have remained limited. Clinical trial information: NCT02773849.

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