MP-04.11

Efficacy and Safety of Intravesical Cretostimogene Grenadenorepvec with Gemcitabine in High-Risk BCG-Exposed Or BCG-Unresponsive Non-Muscle Invasive Bladder Cancer CORE-008 Cohort CX

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BACKGROUND

- Guidelines recommend IVE BCG or RC for HR NMIBC[1,2]
- IVE BCG is associated with variable durability over time, treatment-limiting side effects, and ongoing supply shortages[3-9]
- RC associated with morbidity and complications[10,11]

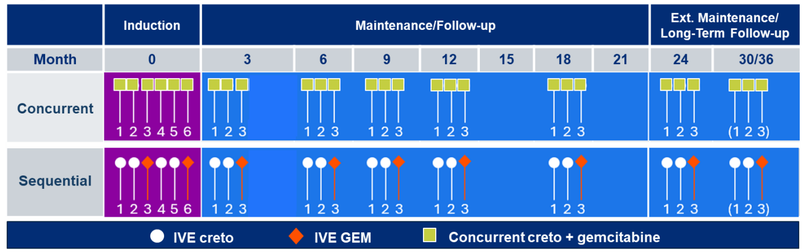
Cretostimogene is an oncolytic immunotherapy with dual mechanisms of action, selectively replicating in and lysing cancer cells while amplifying the immune response against bladder tumors

- CORE-008 is a phase 2, multi-arm, multi-cohort trial evaluating the safety and efficacy of IVE cretostimogene as monotherapy and in combination for HR NMIBC.
- Cohort CX evaluates cretostimogene with gemcitabine in BCG-exposed or BCG-unresponsive NMIBC, leveraging complementary mechanisms of action

METHODS

- Patients randomized to receive IVE cretostimogene and gemcitabine concurrently or sequentially (Figure 1)
- Response assessments: urine cytology, serial cystoscopy, biopsy (as indicated), imaging
- Primary endpoint: HG-EFS (time to first HG recurrence, progression, or death)
- Secondary Endpoints: Safety, CR at Any Time

Figure 1. Study Administration Schedule



Abbreviations: AE, adverse event; BCAN, Bladder Cancer Advocacy Network; BCG, Bacillus Calmette-Guérin; CR, complete response; EFS, event-free survival; GM-CSF, granulocyte-macrophage colony-stimulating factor; HG, high-grade; HR, high-risk; ITT, intention-to-treat; IVE, intravesical; NMIBC, non-muscle invasive bladder cancer; RC, radical cystectomy; SAE, serious adverse event; TRAE, treatment-related adverse event.

CORE-008 COHORT CX

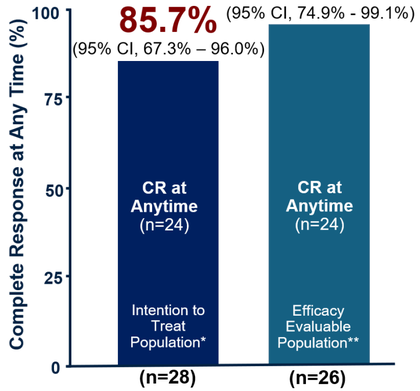
BCAN 20 Years of Impact

Initial Results with Creto + GEM Demonstrate Robust Clinical Activity and Favorable Safety in BCG-Exposed and BCG-Unresponsive NMIBC

RESULTS

- Patients majority: male (78.2%), white (92.7%), >65 years (81.8%)
- All patients enrolled from the U.S. across community (80.0%) and academic (20.0) sites of care
- Median follow up: 6.6 months
- CR rate at any time: 85.7% (ITT); 92.3% (Efficacy; Figure 2)
- ITT CR 83.3% (Concurrent); 87.5% (Sequential)

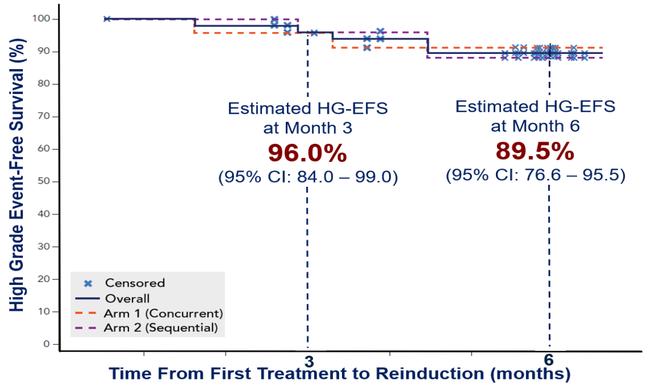
Figure 2. CR at Any Time



Study Arm	CR Rate (95% CI) ITT
1 Concurrent	**83.3%** (51.6, 97.9) *10/12 patients*
2 Sequential	**87.5%** (61.7, 98.5) *14/16 patients*

Acknowledgements: Ying Chen, PhD, Sarah Donatelli, PhD; Sarah Hohl, PhD; Shelja Patel, PharmD; Rob Svatek, MD; Rebecca Tregunna, MD, MBA; and Vijay Kasturi, MD

Figure 3. High-Grade Event Free Survival: ITT Population



Safety Profile

Preferred Term (MedDRA v.26.1)	Overall (n=55)	
	Grade 1-2, n (%)	Grade ≥ 3, n (%)
Patients with ≥ 1 TRAE	36 (65.5 %)	0 (0)
Treatment-Related AE reported in ≥ 20% patients		
Bladder Spasm	26 (47.3)	0 (0)
Dysuria	19 (34.5)	0 (0)
Pollakiuria	14 (25.5)	0 (0)

- 0% Grade ≥ 3 TRAEs, SAEs or deaths
- 85.5% (47/55) completed all protocol-defined treatments
  - Arm 1 (Concurrent)- 71.4% (20/28)
  - Arm 2 (Sequential)- 100% (27/27)
- No patients discontinued on Arm 2 (sequential) due to TRAEs
- 4 withdrew from Arm 1 for persistent grade 1-2 localized TRAEs
- No between-arm differences in proportion of patients with AEs

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References: **1** NCCN Bladder Cancer Guidelines; 2026, **2** AUA/SUO NMIBC Guidelines; 2026 **3** Sylvester,*Eur Urol*; 2006, **4** Kamat,*J Clin Oncol*; 2016, **5** Roumiguie,*Eur Urol*; 2022, **6** Longoni,*Eur Urol Oncol*; 2025, **7** Brausi,*Eur Urol,* 2014, **8** Tapiero,*Urology,*2018, **9** Van Der Meijen,*Eur Urol* 2003, **10** Maibom,*BMJ Open,* 2021, **11** Clements,*Eur Urol* 2021