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# First Results From CORE-008 Cohort CX: Evaluating Intravesical Cretostimogene Grenadenorepvec with Gemcitabine in High-Risk BCG-Exposed or BCG-Unresponsive Non-Muscle Invasive Bladder Cancer

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## BACKGROUND

- Guidelines recommend IVE BCG or radical cystectomy for HR NMIBC[1,2]
- IVE BCG limited by variable durability over time, treatment-limiting side effects, and ongoing supply shortages[3-9]
- Radical cystectomy is 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**

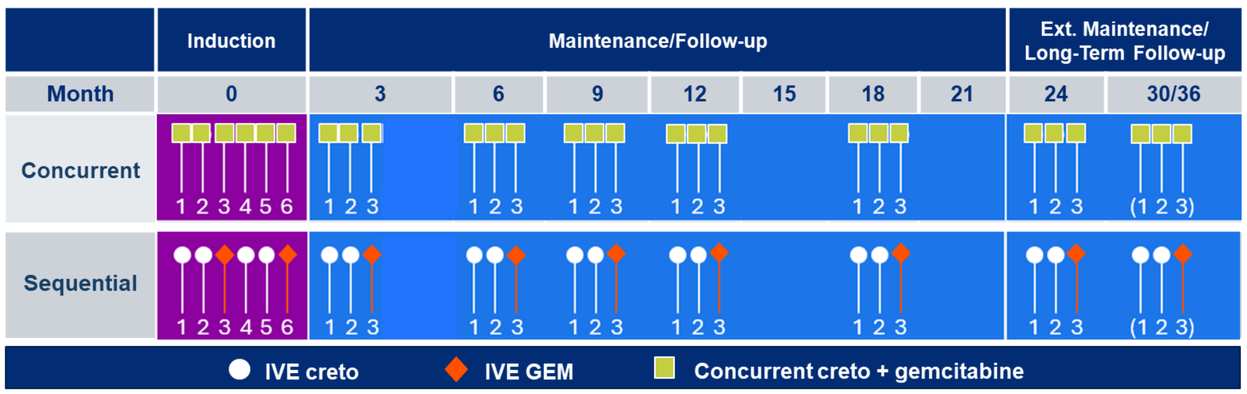
- CORE-008 is a phase 2, multi-arm, multi-cohort trial evaluating the safety and efficacy of intravesical cretostimogene as monotherapy and in rational combinations for HR NMIBC.
- Cohort CX evaluates cretostimogene with intravesical gemcitabine in BCG-exposed or BCG-unresponsive NMIBC, leveraging complementary mechanisms and immune-modulating synergy in an intravesical-only approach.

## METHODS

- HR BCG-exposed or BCG-unresponsive NMIBC patients randomized to receive intravesical cretostimogene and gemcitabine (Figure)
- Response assessments: urine cytology, serial cystoscopy, biopsy (as indicated), imaging
- Primary endpoints: HG-EFS; Secondary Endpoints: Safety, CR at Any Time

| BCG-Exposed | BCG-Unresponsive |
|---|---|
| Patients who had prior BCG and either presented with CIS/HGTa recurrence at first evaluation (BCG-resistant), recurred outside of the BCG-unresponsive window following adequate BCG, or recurred within 24 months after inadequate BCG | Participants who received adequate BCG (5+2) and present with:<br>- HG T1 at first evaluation following induction course<br>- HG Ta/T1 within 6 mo<br>- CIS within 12 mo |

### Study Administration Schedule




## 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
- Median follow up: 6.6 months
- CR rate at any time: 85.7% (ITT); 92.3% (Efficacy)
- ITT CR 83.3% (Concurrent); 87.5% (Sequential)

| 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* |

**Abbreviations:** BCAN: Bladder Cancer Advocacy Network; BCG: Bacillus Calmette-Guerin; EFS: event-free survival; HG: high-grade; HR: high-risk; GM-CSF: granulocyte-macrophage colony-stimulating factor; IVE: intravesical; NMIBC: non-muscle invasive bladder cancer; RC: radical cystectomy; ITT: Intention to treat

**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

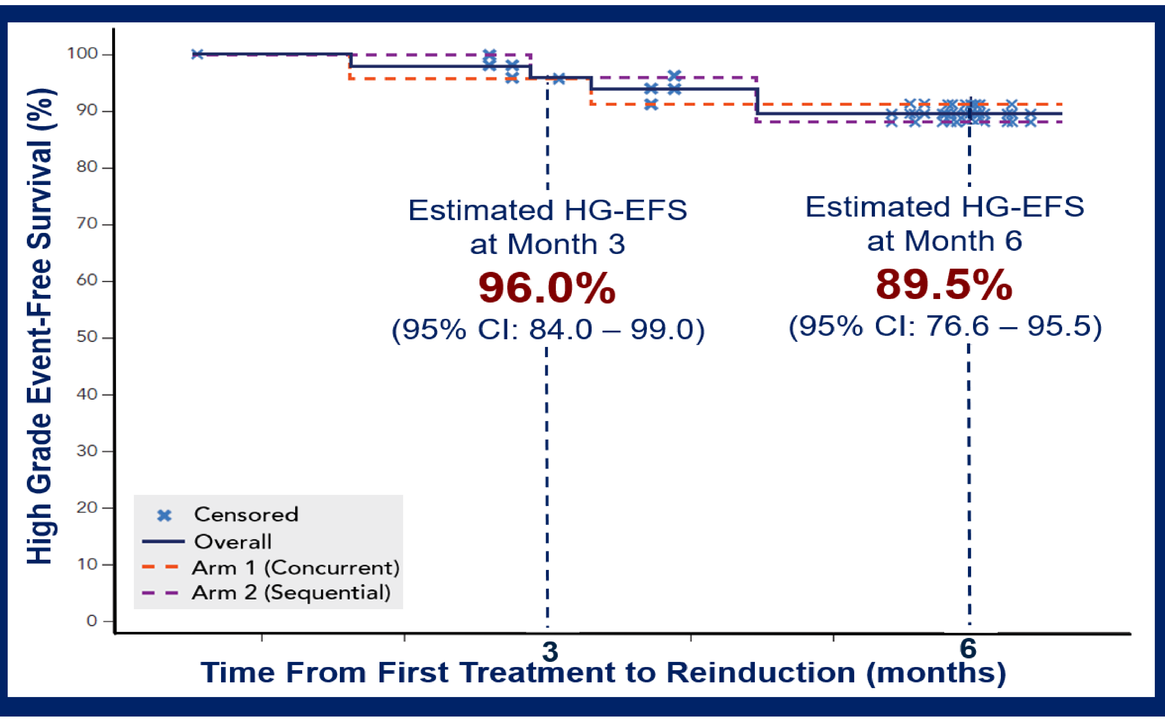
CORE-008 COHORT CX

BCAN 20 Years of Impact

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

## RESULTS

### 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) |
| **Pollakuria** | 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

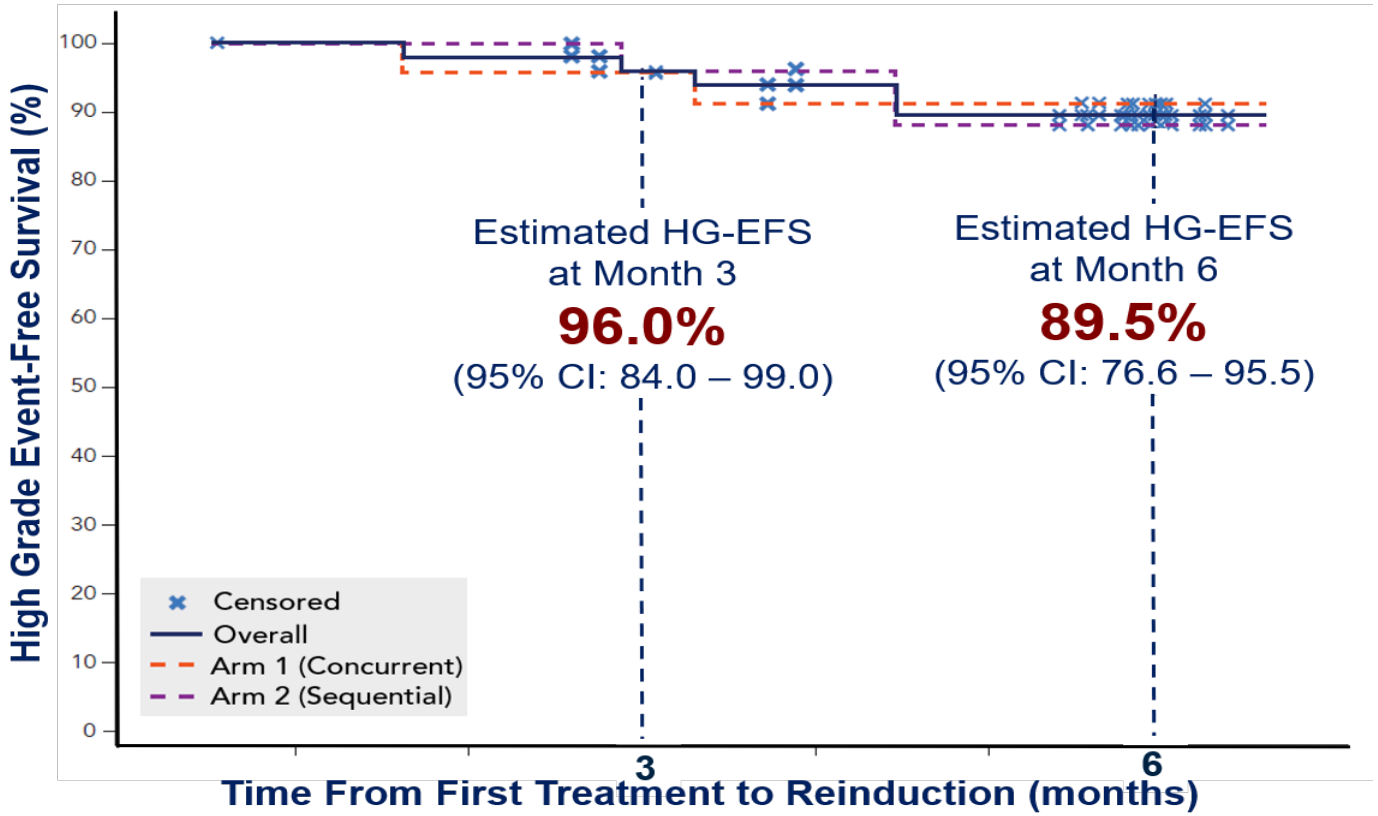
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# #343 First Results From CORE-008 Cohort CX: Evaluating Intravesical Cretostimogene with Gemcitabine in High-Risk BCG-Exposed or BCG-Unresponsive NMIBC

- Patients randomized 1:1 to receive intravesical cretostimogene and gemcitabine concurrently or sequentially
- Primary endpoint: HG-EFS, safety
- Secondary endpoint: CR at any time
- CR rate at any time: 85.7% (ITT); 92.3% (Efficacy)
- ITT CR 83.3% (Concurrent); 87.5% (Sequential)
- 0% Grade ≥ 3 TRAEs, SAEs or deaths

## High Grade Event-Free Survival: ITT population




13MAR2026 data cut

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**Initial results with creto + gem demonstrate clinical activity and favorable safety and tolerability in BCG-exposed and BCG-unresponsive NMIBC**

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