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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

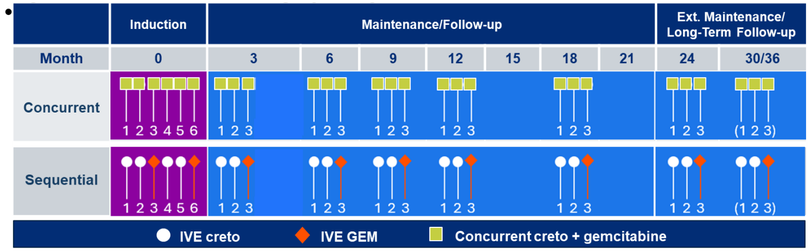
- Guidelines recommend IVE BCG or RC for HR NMIBC[1,2]
- IVE BCG limited by variable durability over time, treatment-limiting side effects, and ongoing supply shortages[3-9]
- RC associated with morbidity and complications[10,11]

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 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-UR NMIBC patients randomized to receive intravesical cretostimogene and gemcitabine (Figure)
- Response assessments: urine cytology, serial cystoscopy, biopsy (as indicated), imaging
- Primary endpoints: HG-EFS



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

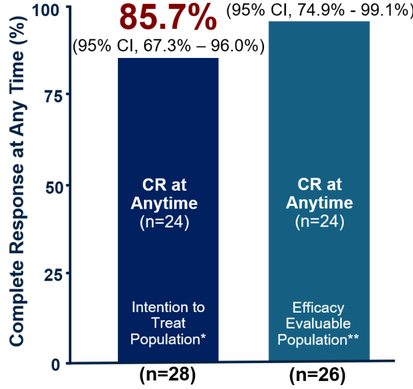
CORE-008 COHORT CX

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

- 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)
- 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*

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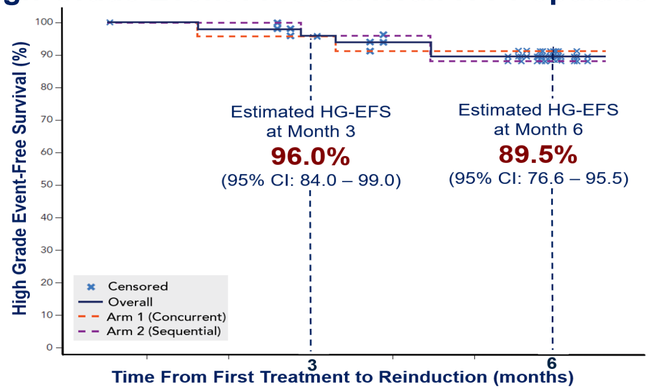
High-Grade Event Free Survival: ITT Population



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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References: **1** NCCN Bladder Cancer Guidelines; 2026, **2** AUA/SUO NMIBC Guidelines; 2024 **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

University of Rochester

Efficacy and Safety of Intravesical Cretostimogene Grenadenorepvec Plus Gemcitabine in High-Risk BCG-Exposed or BCG-Unresponsive Non-Muscle Invasive Bladder Cancer

CORE-008 Cohort CX

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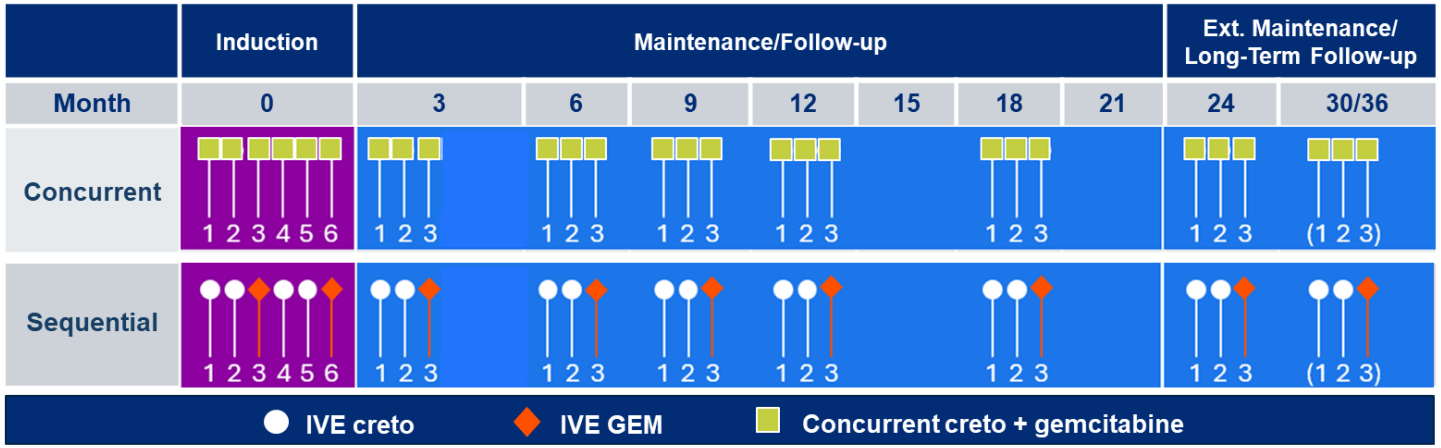
Phase 2 Trial Design and Cohort CX Treatment Schedule



- Re-induction allowed for patients with HG Ta and/or CIS at Month 3
- Assessments include: Cystoscopy & Cytology every 3 months; CT/MRU every 6 months
- Primary endpoint: HG-EFS, Safety
- Secondary endpoint (CIS-containing): CR at Any Time

CIS= Carcinoma in Situ; CR=Complete Response; GEM= Intravesical Gemcitabine; HG-EFS= High-Grade Event-Free Survival
HG-EFS defined as High-grade recurrence/persistence, progression to T1, progression to T2+ and death from any cause. Efficacy assessments based on local pathology review.
Concurrent: Same-day administration of cretostimogene (first) followed by gemcitabine throughout induction and maintenance.
Sequential: Two weekly cretostimogene instillations followed by one gemcitabine instillation (Weeks 1, 2, 4, 5 vs Weeks 3, 6), continued in maintenance.

BCG-Exposed

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

BCG-Unresponsive

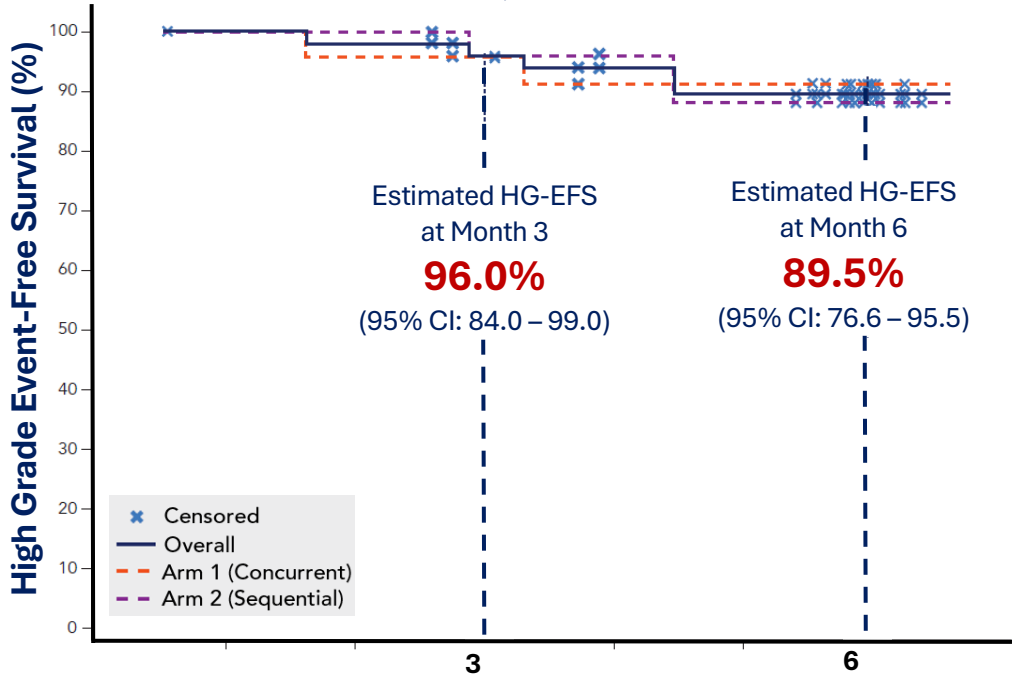
Participants who received adequate BCG (5+2) and present with:

- HG T1 at first evaluation following induction course
- HG Ta/T1 within 6 mo
- CIS within 12 mo

Efficacy in CORE-008 Cohort CX

Primary Endpoint: High-Grade Event-Free Survival

ITT, n=55

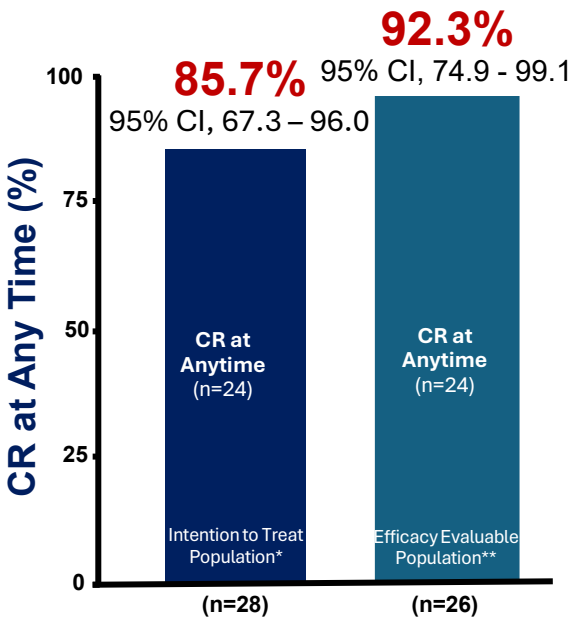


- Demographics: male (78.2%), white (92.7%), >65 years (81.8%), 80% from community sites; median follow-up 6.6 months
- **No significant differences in HG-EFS by arm; consistent response among BCG-UR and BCG-exposed subgroups**
- No treatment-related progression to MIBC or mUC; 2 patients experienced NMIBC stage reclassification

BCG-UR= BCG-Unresponsive; CIS= Carcinoma in Situ; CR= Complete Response; HG-EFS= High-Grade Event-Free Survival; MIBC= Muscle Invasive Bladder Cancer; mUC= Metastatic Urothelial Carcinoma

Secondary Endpoint: CR at Any Time

CIS Containing Population



- High CR rates in both concurrent and sequential arms, with overlapping confidence intervals
- CR outcomes directionally consistent with primary endpoint findings (HG-EFS)

CR Rate	% (n/N)	95% CI
Concurrent	**83.3%** *10 out of 12 patients*	(51.6, 97.9)
Sequential	**87.5%** *14 out of 16 patients*	(61.7, 98.5)

HG-EFS defined as high-grade recurrence/persistence, progression to T1, progression to T2+ and death from any cause. CR defined as having negative cystoscopy, urine cytology, and biopsy (as indicated). CR analysis includes BCG-Exposed and BCG-Unresponsive patients.
Efficacy data cutoff as of 13MAR2026; efficacy assessments based on local pathology review. Two patients with CIS at baseline were found with HG T1 at Mo 6.
*Intention to treat (ITT) population CX (Arm 1/Concurrent; Arm 2/Sequential). **Efficacy evaluable population includes patients who have received at least four doses of cretostimogene, meet the definition of BCG-Unresponsive/BCG-Exposed and have completed a protocol-defined efficacy assessment at Month 3. includes all participants randomized in Cohort

Favorable and Well-Tolerated 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 ≥ 10% patients		
Bladder Spasm	26 (47.3)	0 (0)
Dysuria	19 (34.5)	0 (0)
Pollakuria	14 (25.5)	0 (0)
Fatigue	10 (18.2)	0 (0)
Micturition Urgency	8 (14.5)	0 (0)
Hematuria	6 (10.9)	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 TRAE**
- 4 patients withdrew from Arm 1 (concurrent) for persistent grade 1-2 localized TRAEs
- No difference in the proportion of patients with AEs between arms

AE= adverse events; SAE= Serious adverse events; TRAE=treatment-related adverse events
Safety Data Cutoff Date 13MAR2026
Concurrent: Same-day administration of cretostimogene (first) followed by gemcitabine throughout induction and maintenance.
Sequential: Two weekly cretostimogene instillations followed by one gemcitabine instillation (Weeks 1, 2, 4, 5 vs Weeks 3, 6), continued in maintenance.