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First Results from CORE-008 Cohort CX: Phase 2 Study of Intravesical Cretostimogene Grenadenorepvec with Gemcitabine in Patients with High-Risk BCG-Exposed or BCG-Unresponsive NMIBC

Trinity J. Bivalacqua, MD, PhD

Presented at SUO Annual Meeting at AUA; May 16, 2026; Washington D.C.

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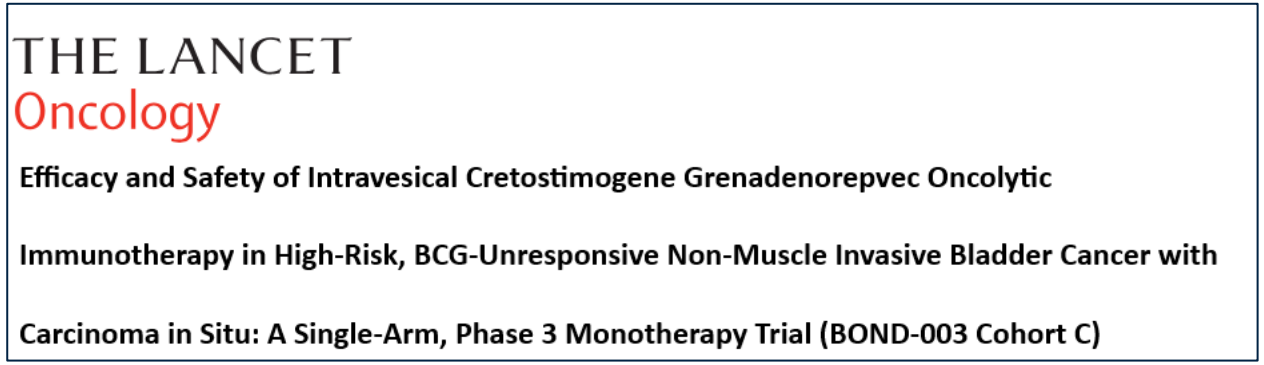
Disclosures

- Grants: NIH SBIR, DOD, RO1, AUA Care Foundation (mentor).
- Clinical trials: CG Oncology, Ferring Pharmaceuticals.
- Scientific Advisory Board: Urogen, CG Oncology, Pfizer.
- Co-Founder: OncoSTING LLC (www.OncoSTING.com).

Rationale for Novel Intravesical Combination Strategies in HR-NMIBC

- Efficacy and safety of cretostimogene monotherapy and in combination with pembrolizumab for HR BCG-UR NMIBC and nivolumab for MIBC have been published.[1-3]
- Novel intravesical therapeutic approaches that leverage complementary mechanisms and immune-modulating synergy are still needed for HR NMIBC.


THE LANCET
Oncology

Efficacy and Safety of Intravesical Cretostimogene Grenadenorepvec Oncolytic Immunotherapy in High-Risk, BCG-Unresponsive Non-Muscle Invasive Bladder Cancer with Carcinoma in Situ: A Single-Arm, Phase 3 Monotherapy Trial (BOND-003 Cohort C)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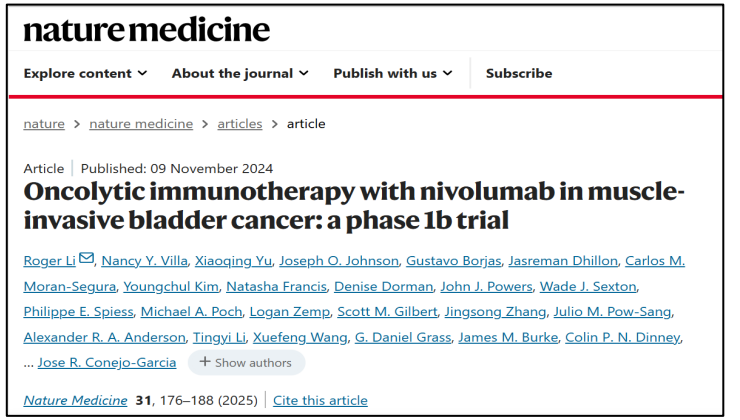
Oncolytic adenoviral therapy plus pembrolizumab in BCG-unresponsive non-muscle-invasive bladder cancer: the phase 2 CORE-001 trial

Roger Li, Paras H. Shah, Tyler F. Stewart, Jong Kil Nam, Trinity J. Bivalacqua, Donald L. Lamm, Edward M. Uchio, Daniel M. Geynisman, Joseph M. Jacob, Joshua J. Meeks, Rian Dickstein, Shane M. Pearce, Seok Ho Kang, Seung Il Jung, Ashish M. Kamat, James M. Burke, Kirk A. Keegan & Gary D. Steinberg

Nature Medicine **30**, 2216–2223 (2024) | Cite this article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Oncolytic immunotherapy with nivolumab in muscle-invasive bladder cancer: a phase 1b trial

Roger Li, Nancy Y. Villa, Xiaoqing Yu, Joseph O. Johnson, Gustavo Borjas, Jasreman Dhillon, Carlos M. Moran-Segura, Youngchul Kim, Natasha Francis, Denise Dorman, John J. Powers, Wade J. Sexton, Philippe E. Spiess, Michael A. Poch, Logan Zemp, Scott M. Gilbert, Jingsong Zhang, Julio M. Pow-Sang, Alexander R. A. Anderson, Tingyi Li, Xuefeng Wang, G. Daniel Grass, James M. Burke, Colin P. N. Dinney, ... Jose R. Conejo-Garcia + Show authors

Nature Medicine **31**, 176–188 (2025) | Cite this article

IVE=intravesical

1. Tyson M, et al. *Lancet Oncology* 2026. 2. Li R, et al. *Nat Med* 2024;30(8):2216-2223 3. Li, R, et al. *Nat Med* 2025; 31(1):176-188

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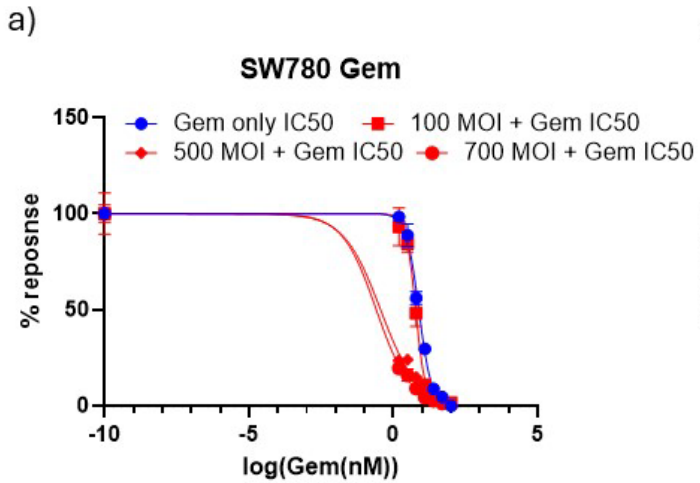
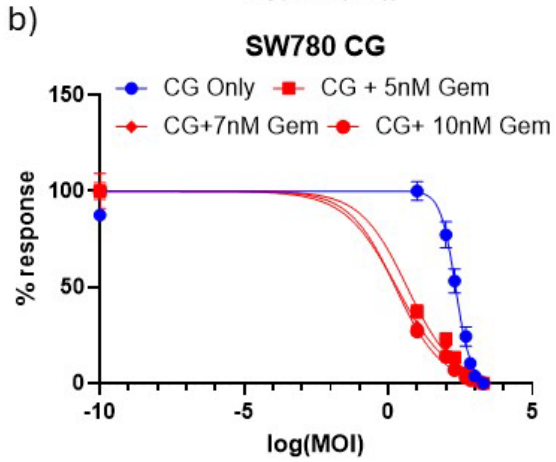
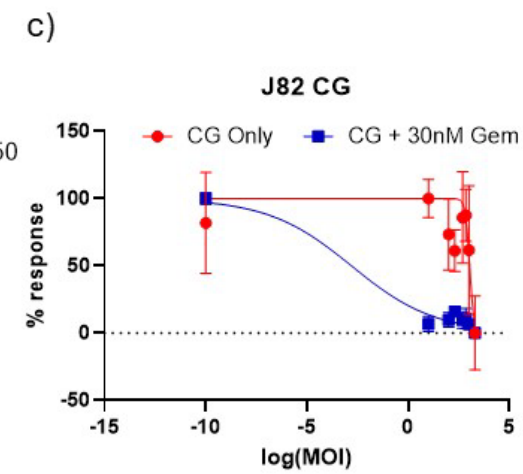
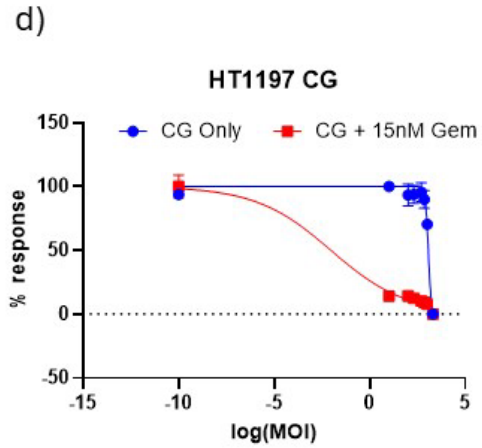
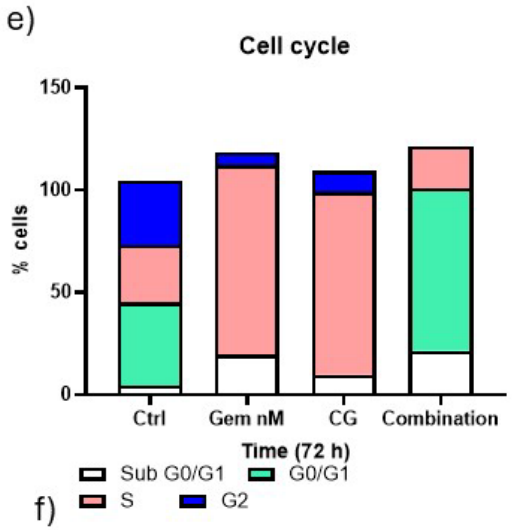
Gemcitabine Enhances the Anti-Tumor Activity of Cretostimogene

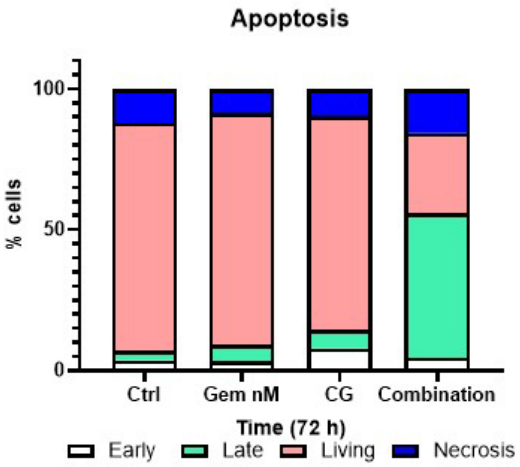








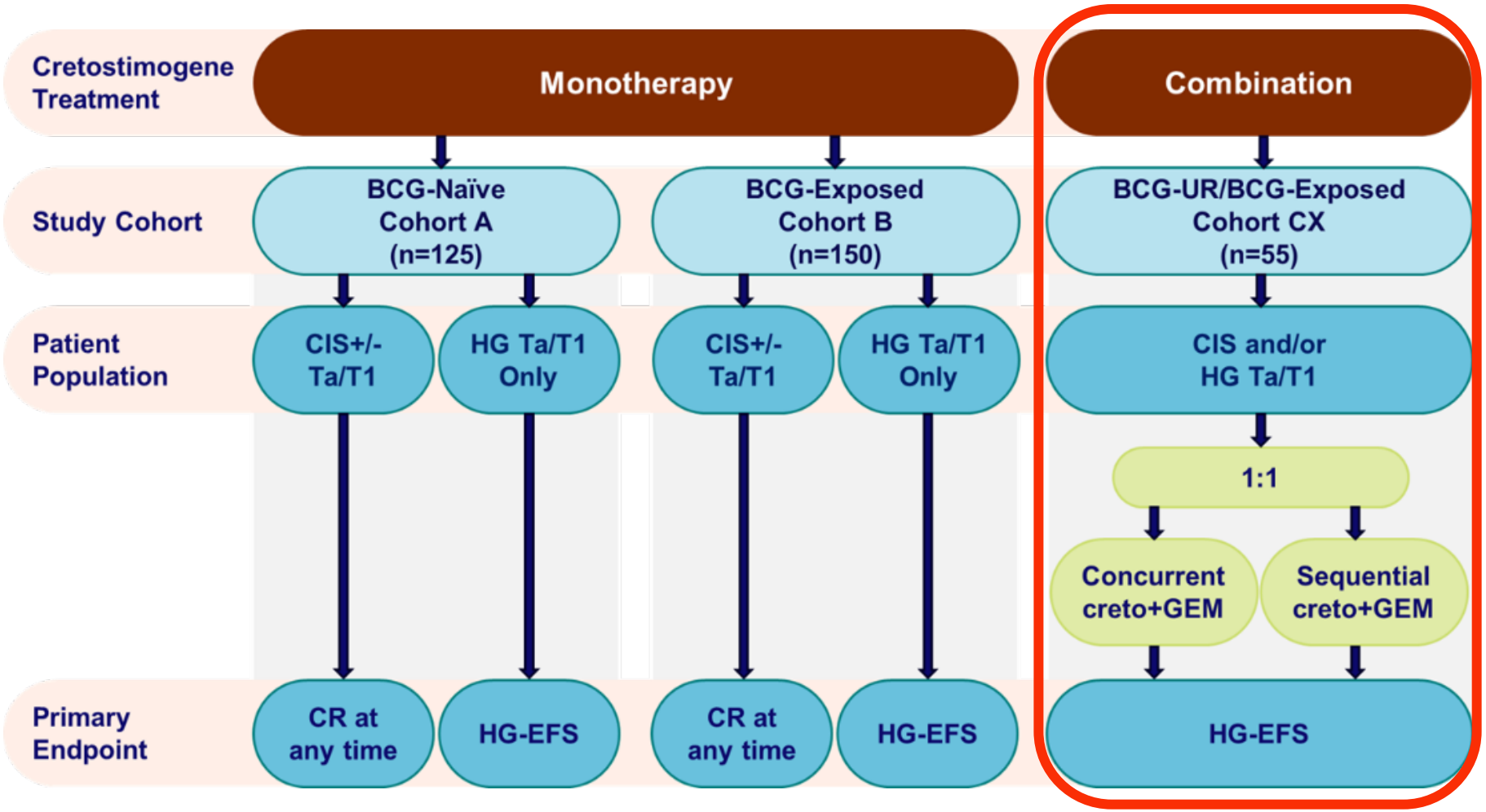




- Enhanced in-vitro response to cretostimogene when combined with gemcitabine.
- Increased G0/G1 cell-cycle arrest and apoptosis.

Steinmetz, Tholmier, Martini, and Mokkapati, 2025 (unpublished data).

CORE-008: Phase 2, Multi-Cohort Trial in HR NMIBC



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

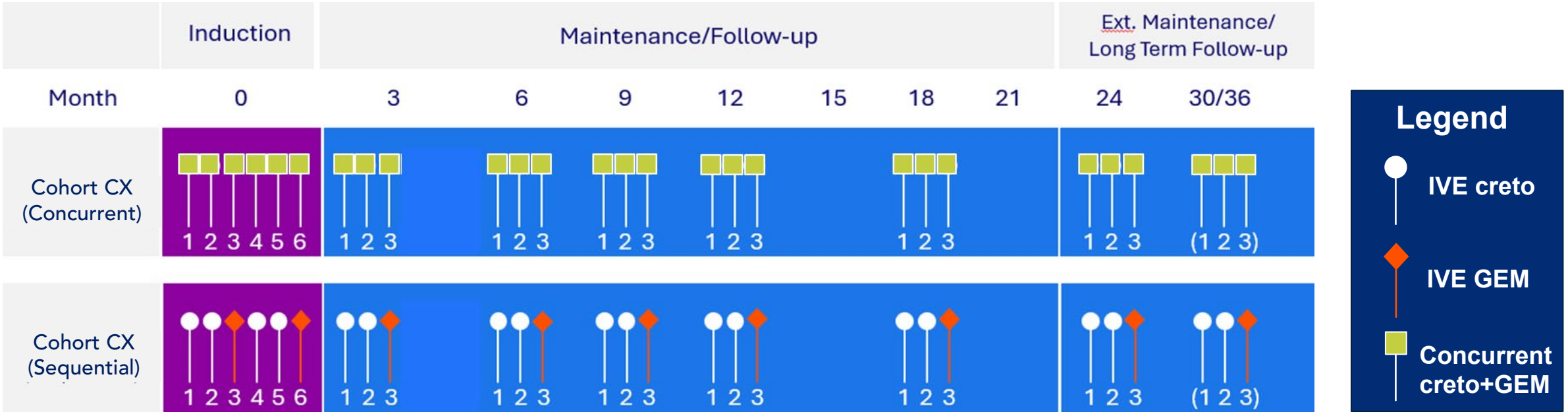
BCG-Unresponsive

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

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
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.

Treatment & Assessment 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
- Clinic-based instillation with flexibility to void at home after instillation during maintenance

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.
Efficacy assessments based on local pathology review.

Patient Demographics & Baseline Characteristics

Patients in Safety Dataset	N=55	%
Gender		
Male	43	78.2
Female	12	21.8
Age (Years)		
Mean (Range)	73.1 (54-88)	
Median (IQR)	75 (66-79)	
Age (Categories)		
< 65	10	18.2
≥ 65 and < 75	17	30.9
≥75	28	50.9
ECOG PS		
0	48	87.3
1	6	10.9
2	1	1.8
HR NMIBC T-Stage at Study Entry		
CIS +/- HG Ta/T1	28	50.9
HG Ta/T1	27	49.1
BCG History, n (%)		
Median BCG doses (IQR)	7.0 (6-13)	
BCG-Exposed	36	65.5
BCG-Unresponsive	19	34.5

- All patients enrolled from the U.S. across multiple sites of care
  - 80.0% community
  - 20.0% academic
- **Majority of patients are:**
  - Male (78.2%)
  - White (92.7%)
  - > 65 years (81.8%)
- **Cohort generally well-balanced across concurrent and sequential treatment arms**

Efficacy data cutoff as of 13MAR2026.

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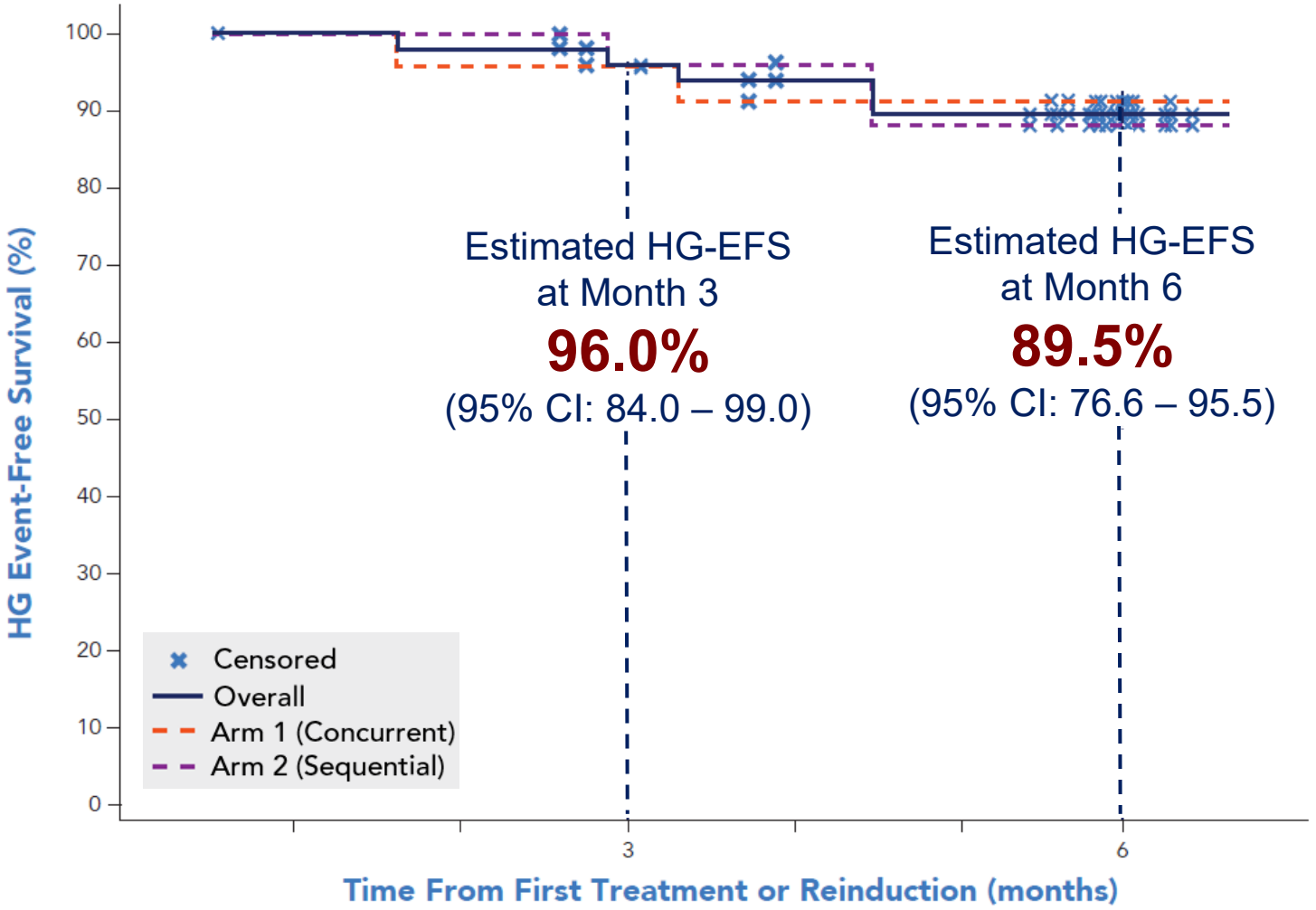
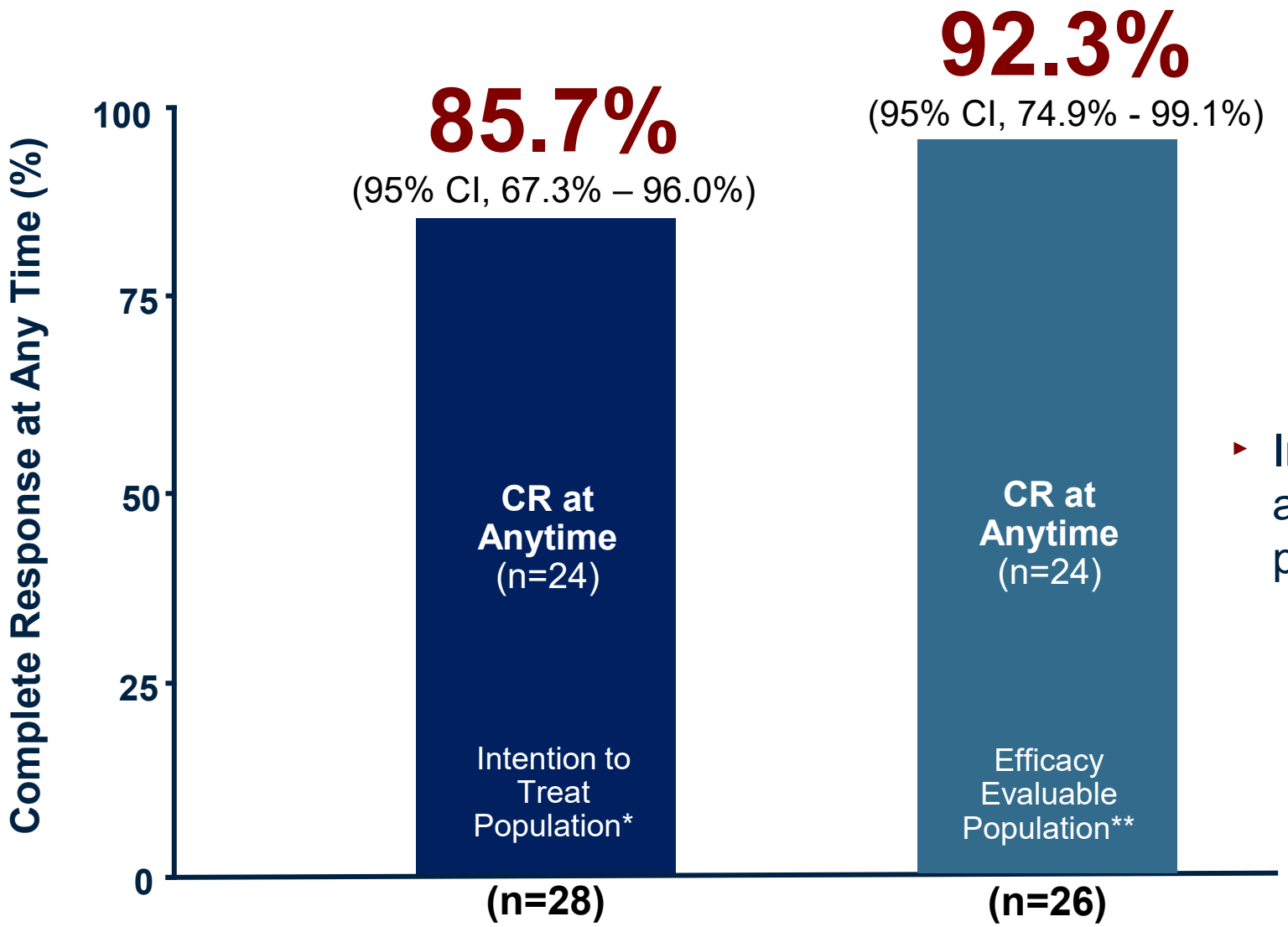
High-Grade Event-Free Survival at 3 and 6-Months From CORE-008 Cohort CX (ITT Population)



- 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; HG-EFS= High-Grade Event-Free Survival; MIBC= Muscle Invasive Bladder Cancer; mUC= Metastatic Urothelial Carcinoma; HG-EFS defined as high-grade recurrence/persistence, progression to T1, progression to T2+ and death from any cause; Efficacy data cutoff as of 13MAR2026; Efficacy assessments based on local pathology review; HG-EFS presented in intention to treat (ITT) population representative of all patients randomized on CORE-008 Cohort CX (Arm 1/Concurrent; Arm 2/Sequential); Two patients with CIS at baseline were found with HGT1 at Month 6.

High Complete Response Rates Within CIS-Containing Population



- Includes BCG-Exposed and BCG-Unresponsive patients

CIS= Carcinoma in Situ; CR=Complete Response
CR defined as having negative cystoscopy, urine cytology, and biopsy (as indicated).
Efficacy data cutoff as of 13MAR2026. Efficacy assessments based on local pathology review.
* Intention to treatment (ITT) population includes all participants who are randomized in Cohort 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

Complete Response Rates Maintained Across Treatment Arms Within CIS-Containing ITT Population

CR Rate	% (n/N)	Confidence Interval (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)

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

CIS= Carcinoma in Situ; CR= Complete Response
Efficacy data cutoff as of 13MAR2026; Efficacy assessments based on local pathology review.
Intention to treatment (ITT) population includes all participants who are randomized in Cohort CX (Arm 1/Concurrent; Arm 2/Sequential).

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.

CORE-008 Cohort CX: Summary and Conclusions

- The combination of cretostimogene and gemcitabine demonstrates **robust clinical efficacy and safety** in BCG-exposed and BCG-unresponsive NMIBC
- **Comparable efficacy** observed in both concurrent and sequential arms
- Sequential administration of intravesical cretostimogene and gemcitabine was **well-tolerated** and supports the feasibility of intravesical-only treatment strategies
- **Continued follow-up is underway** to further characterize longer-term outcomes

Cohort CX Insights Shaping Phase 3 Trial Under Consideration by SWOG

A Randomized Comparison of Intravesical Therapies:
A phase 3 study of cretostimogene grenadenorepvec/gemcitabine (CRETO-GEM) versus gemcitabine/Docetaxel (GEM DOCE) for the treatment of BCG-unresponsive NMIBC

Mark Tyson
Professor of Urology
Mayo Clinic

Sunday, May 17, 2026 9:08 AM to 9:16 AM America/New York

Hall B, The Square, Learning Lab

Learning Lab

CORE-008
COHORT CX

BCAN
20 Years of Impact

Thank You

All Bladder Cancer Patients and Their Families

Key Investigators, Study Coordinators, Nurses

Key Collaborators

Aaron Berger, Associated Urologic Specialists, Chicago Ridge, IL

Mark Tyson, Mayo Clinic, Phoenix, AZ

Christopher Pieczonka, AMP, Syracuse, NY

Jason Hafron, Michigan Institute of Urology, West Bloomfield, MI

Kyle Rose, Oschner Medical Center, New Orleans, LA

Gary Steinberg, Rush University, Chicago, IL

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CG Oncology

Ying Chen

Pat Keegan

Sarah Donatelli

Sarah Hohl

Shelja Patel

Rob Svatek

Rebecca Tregunna

Vijay Kasturi

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First Results From CORE-008 Cohort CX: Phase 2 Study of Intravesical Cretostimogene Grenadenorepvec with Gemcitabine in Patients with High-Risk BCG-Exposed or BCG-Unresponsive NMIBC

Trinity J. Bivalacqua, MD, PhD;[1*] Aaron Berger, MD;[2] Mark D. Tyson, MD, MPH;[3] Christopher M. Pieczonka, MD;[4] Jason Hafron, MD;[5] Kyle Rose, MD;[6] Gary D. Steinberg, MD;[7] Siamak Daneshmand, MD;[8] and Colin P.N. Dinney, MD[9]

[1]University of Pennsylvania, Philadelphia, Pennsylvania [2]Associated Urological Specialists, Chicago Ridge, Illinois [3]Mayo Clinic, Phoenix, Arizona [4]Associated Medical Professionals, Syracuse, New York [5]Michigan Institute of Urology, West Bloomfield, Michigan [6]Oschner Medical Center, New Orleans, Louisiana [7]Rush University Medical Center, Chicago, Illinois [8]University of Southern California, Los Angeles, California [9]University of Rochester, Rochester, New York

BACKGROUND

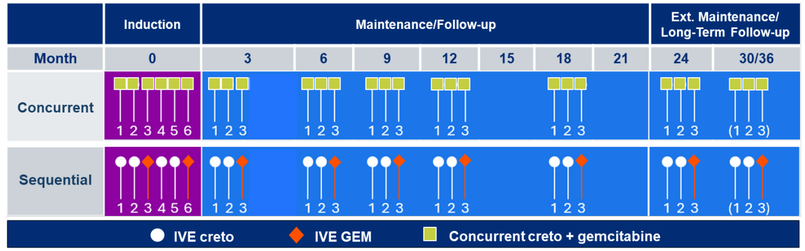
- Guidelines recommend IVE BCG or RC for HR NMIBC[1,2]
- IVE BCG limited by variable durability over time, treatment-limiting side effects, and ongoing supply shortages[3-9]
- RC associated with morbidity and complications[10,11]

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
- Co-primary endpoints: HG-EFS and Safety



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

CORE-008 COHORT CX

Initial results with CRETO+GEM demonstrate clinical activity and favorable safety and tolerability in BCG-Exposed and BCG-Unresponsive NMIBC

Additional data, including per-arm results, will be presented during the SUO at AUA oral session

BASELINE CHARACTERISITCS

- Patients primarily: 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
- Cohort well-balanced across concurrent and sequential arms

Patients in Safety Dataset	N=55	%
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BCG History, n (%)		
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BCG-Exposed	36	65.5
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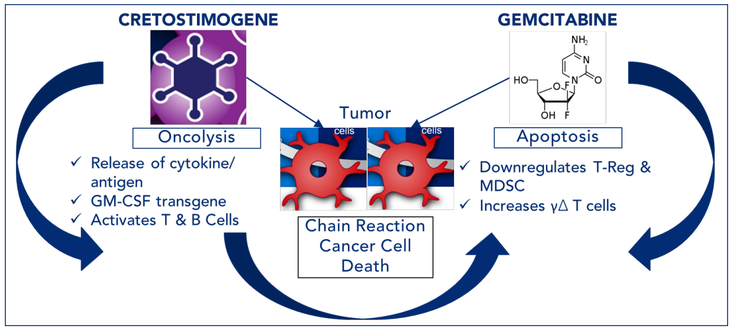
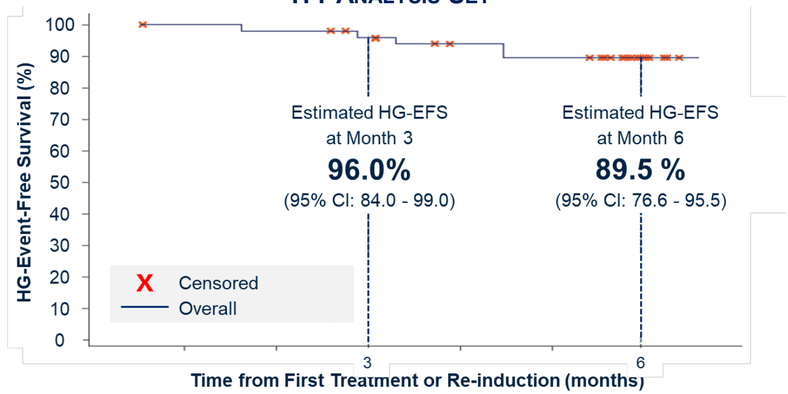
MECHANISM OF ACTION



RESULTS

- As of March 13, 2026, median follow up: 6.6 months
- Overall HG-EFS: 96.0% at 3 months, 89.5% at 6 months

KAPLAN-MEIER PLOT OF HIGH-GRADE EVENT FREE SURVIVAL
ITT ANALYSIS SET



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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

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