G08

First Results From CORE-008 Cohort A: Phase 2 Study of Intravesical Cretostimogene Grenadenorepvec in Patients with High-Risk, BCG-Naive Non-Muscle Invasive Bladder Cancer

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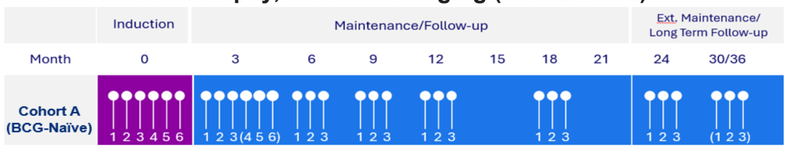
BACKGROUND

- Guidelines currently recommend IVE BCG or RC for HR NMIBC[1,2]
- Challenges with IVE BCG: variable durability across historical vs contemporary studies, treatment-limiting side effects, and ongoing supply shortages[3-9]
- RC carries substantial morbidity and complications[10,11]
- Cretostimogene is an oncolytic immunotherapy with dual mechanisms of action; it selectively replicates in and lyses cancer cells while simultaneously amplifying the immune response against bladder tumors
- CORE-008 is a phase 2, multi-arm, multi-cohort, open-label trial to evaluate the safety and efficacy of cretostimogene across a broad HR NMIBC population

METHODS

- Cohort A includes HR BCG-Naïve NMIBC with CIS, defined as no prior BCG, BCG administered >24 months ago, or receipt of only 1-2 BCG doses within the past 24 months
- Randomized 1:1:
  - Original (5-step): saline wash → DDM wash→ DDM dwell → saline wash→ cretostimogene dwell
  - Optimized (2-step): DDM→ cretostimogene dwell
- Response assessments included urine cytology, serial cystoscopy with directed biopsy, and axial imaging (as indicated)



Abbreviations: BCAN= Bladder Cancer Advocacy Network; CR = complete response; DoR= duration of response; HG= high-grade; HR= high-risk; NMIBC = non-muscle invasive bladder cancer; RC= radical cystectomy; TRAE = treatment-related adverse event

References: **1** NCCN Bladder Cancer Guidelines; 2025, **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

Acknowledgements: Sarah Donatelli, PhD; Pat Keegan, MD; Rob Svatek, MD; Rebecca Tregunna, MD, MBA; Shelja Patel, PharmD and Vijay Kasturi, MD

SUO CTC Society of Urologic Oncology Clinical Trials Consortium, Inc.

CORE-008 COHORT A

BCAN 20 Years of Impact

Initial Results in BCG-Naïve NMIBC

Flexibility Permitted with Optimized (2-step) Administration

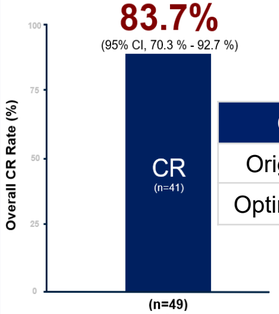
Additional Treatment Arms Planned

BASELINE CHARACTERISITCS

- Majority of patients are: Male (90.7%), White (92.6%), >65 years (88.8%)
- All patients enrolled from the U.S.
- Well balanced across original vs optimized administration approaches

Patients in Safety Dataset	N=54	%
ECOG PS		
ECOG PS 0	44	81.5
ECOG PS 1	10	18.5
HR NMIBC T-Stage at Study Entry		
CIS alone	24	44.4
CIS with HG Ta	17	31.5
CIS with HG T1	13	24.1
BCG History, n (%)		
No Prior BCG	47	87.0
BCG >24 Mo Ago	7	13.0
Prior Adjuvant IVE Chemotherapy, n (%)		
Adjuvant IVE Chemotherapy	7	13.0
No Adjuvant IVE Chemotherapy	47	87.0

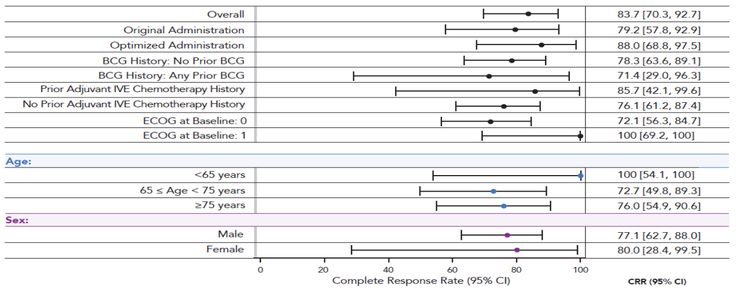
RESULTS



CR Rate	% (n/N)	95% CI
Original Admin	**79.2%** (19/24)	(57.8, 92.9)
Optimized Admin	**88.0%** (22/25)	(68.8, 97.5)

- As of Sept 01, 2025- Median follow-up 4.6 months
- No patients required radical cystectomy
- No treatment-related progression to MIBC or mUC
- 3 patients experienced NMIBC stage reclassification

CONSISTENT TREATMENT EFFECTS



SAFETY PROFILE

- 0% Grade ≥ 3 TRAEs, SAEs or deaths
- No treatment related discontinuations
- 98.1% (53/54) completed all protocol-defined treatments
  - Original Admin 96.3% (26/27)
  - Optimized Admin 100% (27/27)

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