#143 Clinical and Pharmacokinetic/Pharmacodynamic Insights from CORE-008 Cohort A: Phase 2 Study of Intravesical Cretostimogene Grenadenorepvec in Patients with High-Risk BCG-Naïve Non-Muscle Invasive Bladder Cancer

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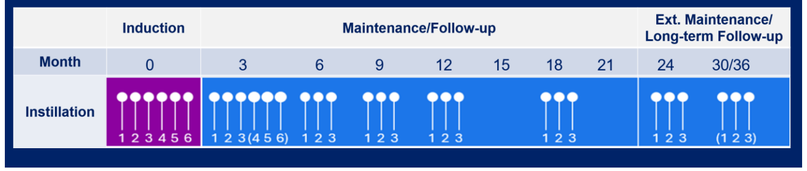
BACKGROUND

- Guidelines recommend IVE BCG or RC for HR NMIBC[1,2]
- IVE BCG challenges: variable durability across literature, treatment-limiting side effects, ongoing supply shortages[3-9]
- RC carries substantial morbidity and complications[10,11]
- Cretostimogene is an oncolytic immunotherapy with dual mechanisms of action that 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 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 (no prior BCG, BCG >24 months ago)
- Randomized 1:1:
  - Original (5-step): saline wash → DDM wash→ DDM dwell → saline wash→ cretostimogene dwell
  - Optimized (2-step): DDM→ cretostimogene dwell
- Response assessments: urine cytology, serial cystoscopy with directed biopsy, axial imaging (as indicated)
- Primary endpoint: CR at any time

STUDY ADMINISTRATION SCHEDULE



Abbreviations: IVE= Intravesical; 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; MIBC= muscle invasive bladder cancer; mUC= metastatic urothelial cancer; SAE= serious adverse event;TRAE = treatment-related adverse event

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

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SUO CTC Society of Urologic Oncology Clinical Trials Consortium, Inc. | CORE-008 COHORT A | BCAN 20 Years of Impact

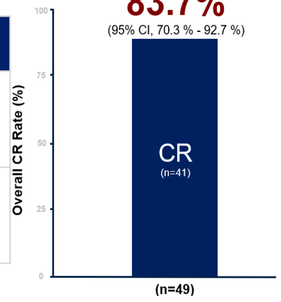
Initial, Clinical Results in BCG-Naïve NMIBC

Translational Insights Reinforce Cretostimogene's MOA, Treatment Schedule, and Safety Profile

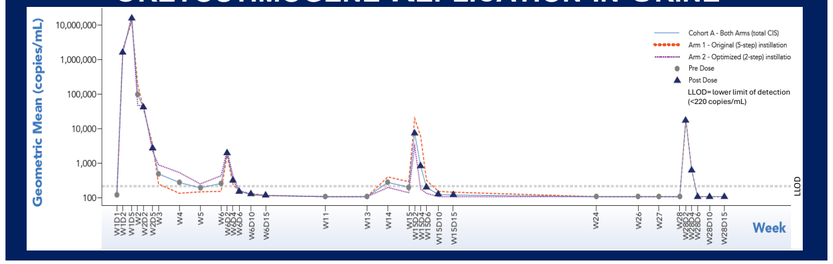
RESULTS

- Majority of patients are: Male (90.7%), White (92.6%), >65 years (88.8%)
- As of Sept 01, 2025: Median follow-up 4.6 months; 83.7% overall CR
- Consistent treatment effect across patient subgroups
- No patients required radical cystectomy
- No treatment-related progression to MIBC or mUC; 3 patients experienced NMIBC stage reclassification
- 0% Grade ≥ 3 TRAEs, SAEs or deaths; No tx-related discontinuations

CR Rate	% (n/N)	95% CI
Original Admin **(5-Step)**	**79.2%** (19/24)	(57.8, 92.9)
Optimized Admin **(2-Step)**	**88.0%** (22/25)	(68.8, 97.5)

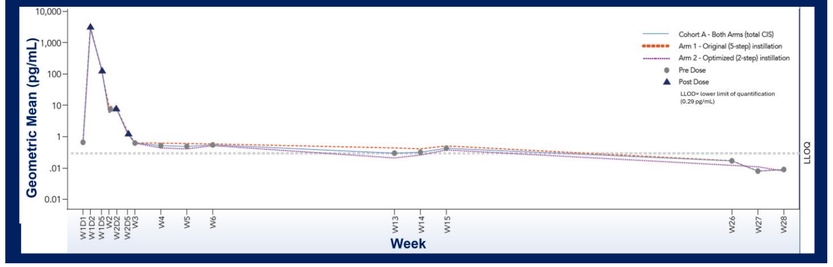


CRETOSTIMOGENE REPLICATION IN URINE



- No detectable cretostimogene levels and low endogenous GM-CSF in the urine of the 53 patients' samples tested at baseline
- Transient increase in cretostimogene levels during induction, declining below the limit of detection after induction and maintenance dosing, with no evidence of latent or extended replication
- No appreciable differences in viral levels between arms
- Consistent with findings from BOND-003 Cohort C (BCG-UR with CIS)
- Effective viral clearance supports relaxed close-contact precautions

GM-CSF TRANSGENE EXPRESSION IN URINE



- GM-CSF levels increased robustly after first induction dose; declined to near-baseline levels within a week, indicating successful transgene expression
- Maintenance GM-CSF remain near baseline, consistent with transient expression and pre-dose sampling
- No substantial differences in GM-CSF levels between arms
- Transient GM-CSF expression aligns with intended MOA

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