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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 shortages³⁻⁹
- 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

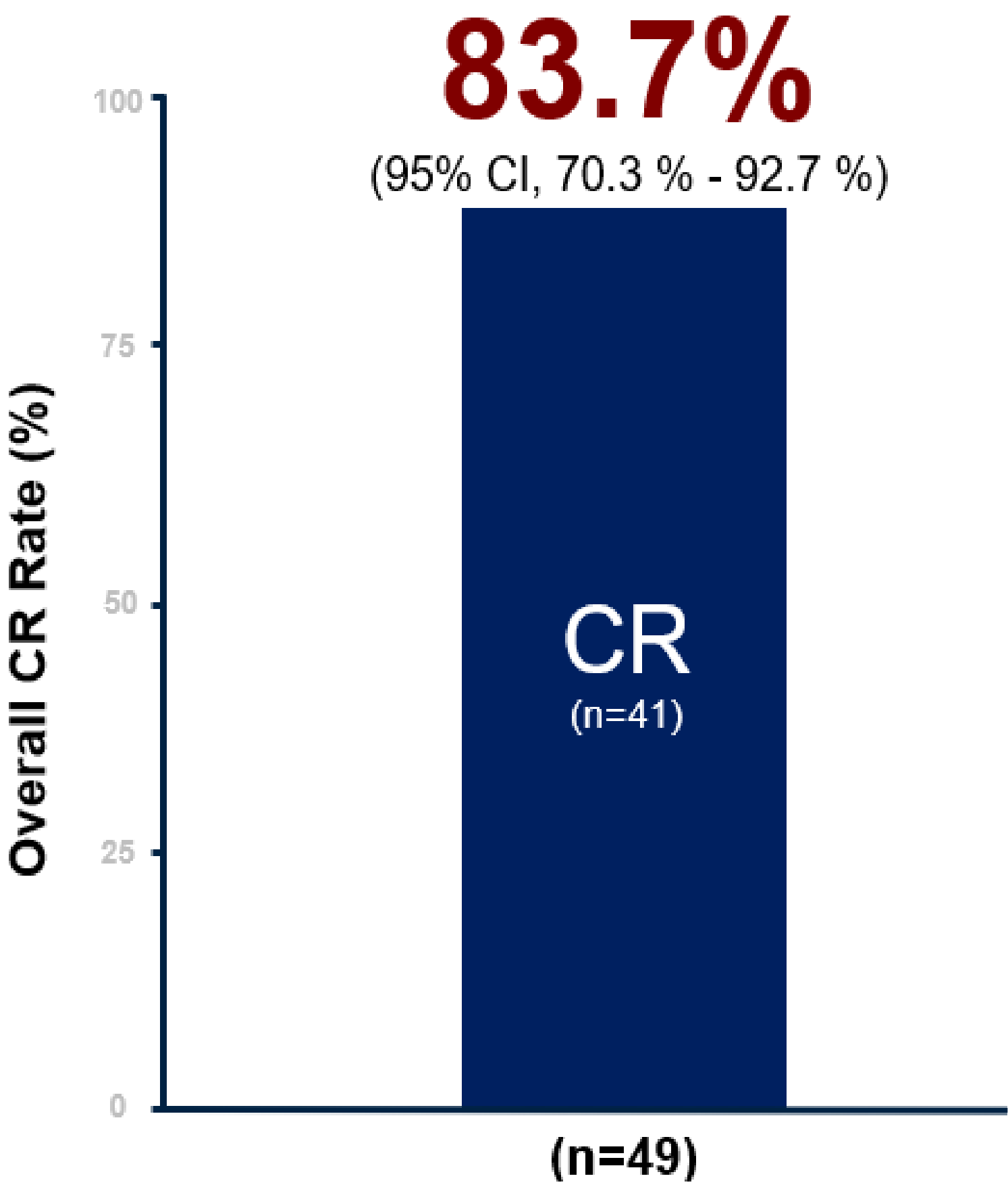
- Cohort A includes HR BCG-Naïve NMIBC with CIS (no prior BCG, BCG >24 months ago)
- Randomized 1:1:
 - Original (5-step): saline wash → DDM wash→ DDM dwell → saline wash→ cretostimogene dwell
 - Optimized (2-step): DDM wash→ cretostimogene dwell
- Response assessments: urine cytology, serial cystoscopy with directed biopsy, axial imaging (as indicated)
- Primary endpoint: CR at any time

STUDY ADMINISTRATION SCHEDULE												
	Induction		Maintenance/Follow-up							Ext. Maintenance/ Long-term Follow-up		
Month	0		3	6	9	12	15	18	21	24	30/36	
Instillation	<div><div></div><div></div><div></div><div></div><div></div><div></div></div>		<div><div></div><div></div><div></div><div></div><div></div><div></div></div>		<div><div></div><div></div><div></div></div>		<div><div></div><div></div><div></div></div>		<div><div></div><div></div><div></div></div>		<div><div></div><div></div><div></div></div>	
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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)



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

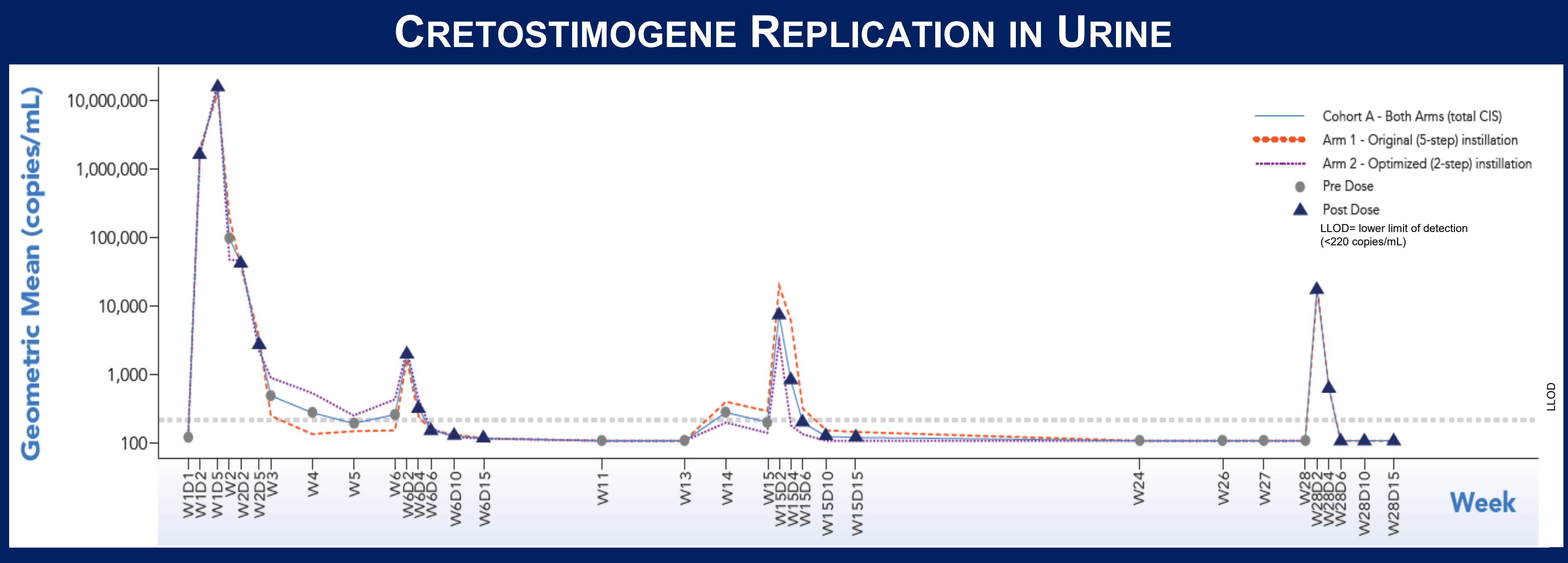
References: 1 NCCN Bladder Cancer Guidelines; 2026, 2 AUA/SUO NMIBC Guidelines; 2026 3 Sylvester,*Eur Urol*; 2006, 4 Kamat,*J Clin Oncol*; 2016, 5 Roumiguie,*Eur Urol*; 2022, 6 Longoni,*Eur Urol Oncol*; 2025, 7 Brausi,*Eur Urol*, 2014, 8 Tapiero,*Urology*,2018, 9 Van Der Meijen,*Eur Urol* 2003, 10 Maibom,*BMJ Open*, 2021, 11 Clements,*Eur Urol* 2021

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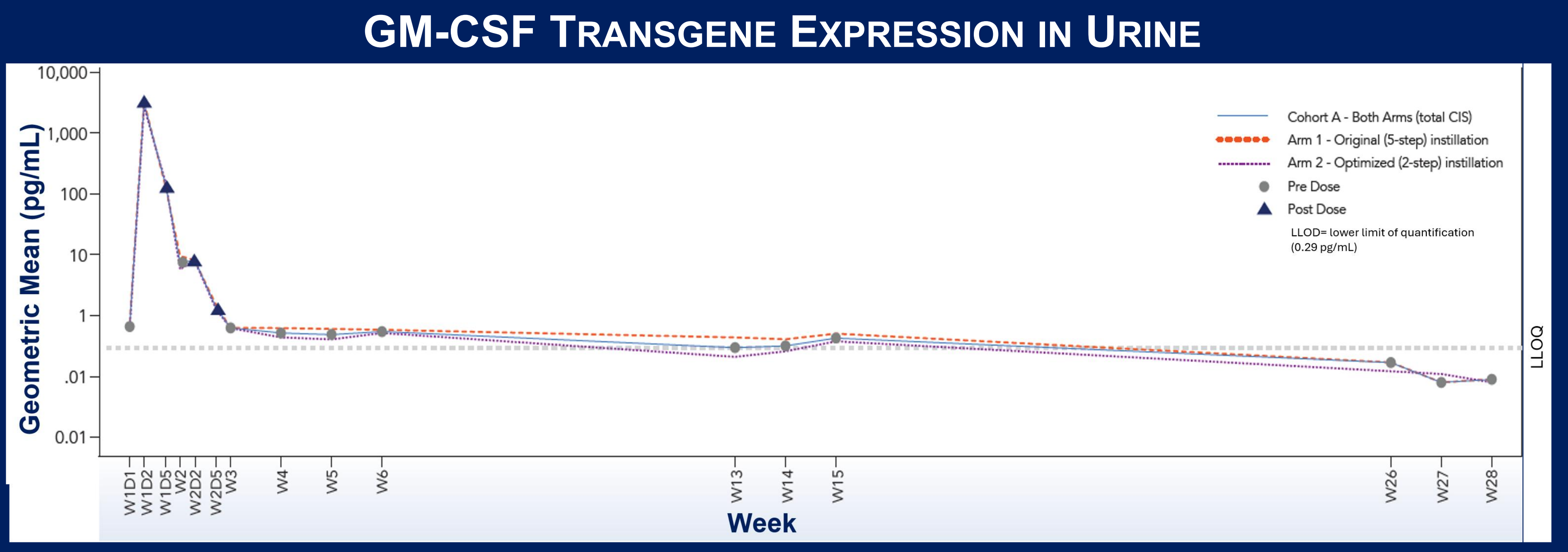


Initial, Clinical Results in BCG-Naïve NMIBC Translational Insights Reinforce Cretostimogene’s MOA, Treatment Schedule, and Safety Profile

RESULTS



- 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 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

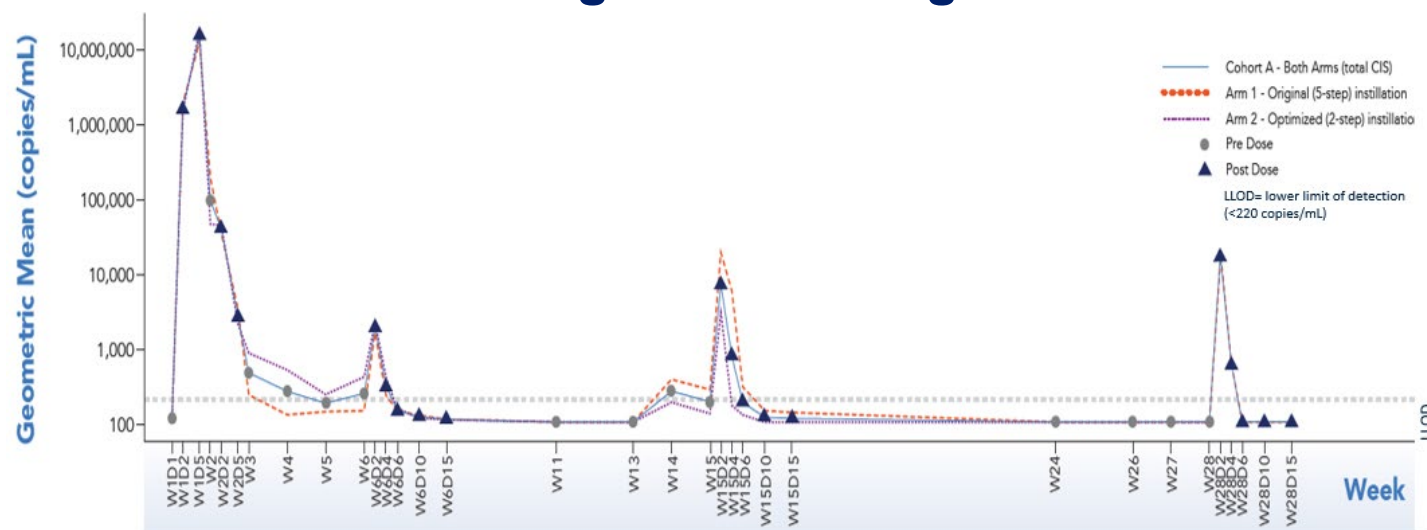
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Clinical and Pharmacokinetic/Pharmacodynamic Insights from CORE-008 Cohort A: Phase 2 Study of Cretostimogene in Patients with High-Risk BCG-Naïve NMIBC

- Patients with HR BCG-Naïve NMIBC with CIS randomized:
 - Original (5-step) administration
 - Optimized (2-step) administration
- Overall CR: 83.7% (95% CI: 70.3, 92.7)
- 90.1% completed all protocol-defined treatments (Optimized admin: 100%)
- 0 grade ≥ 3 TRAEs
- GM-CSF levels increased robustly after first induction dose, indicating successful transgene expression
- No detectable cretostimogene and low endogenous GM-CSF

01Sept2025 data cut off

Cretostimogene Shedding in Urine



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



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