

First Results from CORE-008 Cohort A: Phase 2 Study of Intravesical Cretostimogene Grenadenorepvec in Patients with High-Risk BCG-Naïve NMIBC

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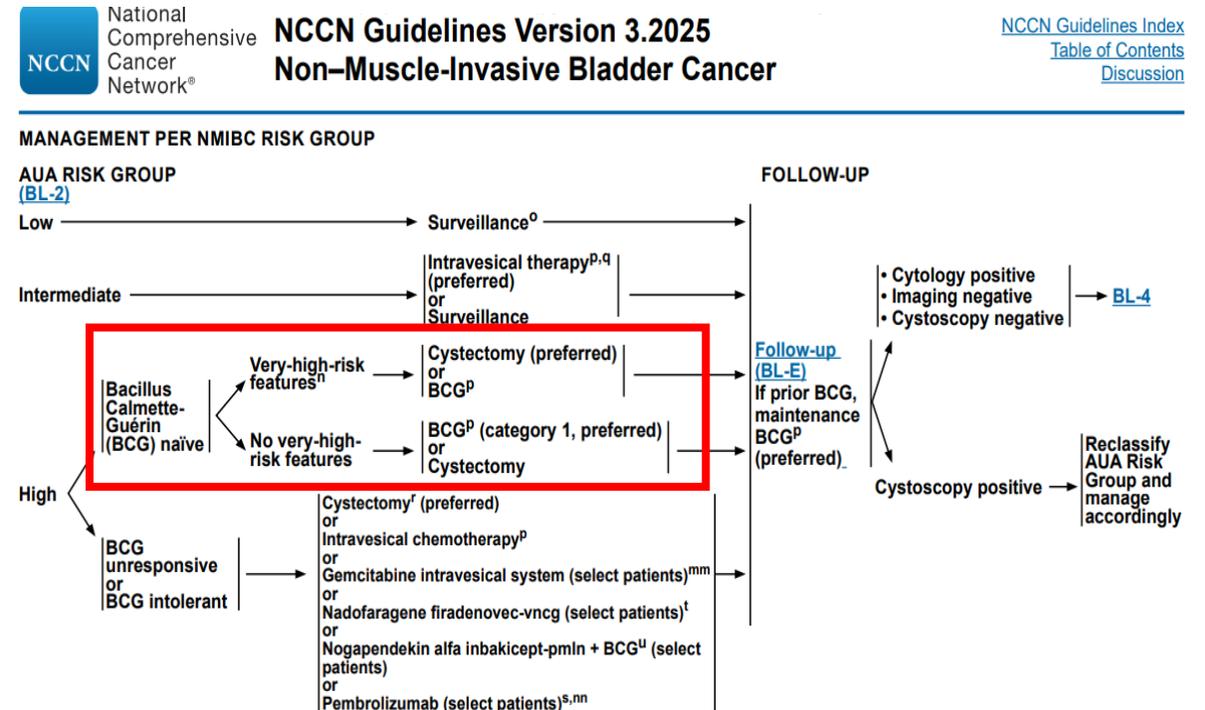
Disclosures

- CG Oncology- No Conflicts of Interest



Considerable Unmet Needs in High-Risk NMIBC

- Guidelines currently recommend IVE BCG or radical cystectomy
- Challenges with BCG**
 - While BCG demonstrates strong initial efficacy, durability remains a challenge
 - Historical data report over 50% of patients recur and 20-40% are at risk for progression¹⁻³
 - Contemporary outcomes demonstrate improved durability with 3-yr EFS/DFS $\geq 75\%$ ⁴
 - 70% of patients experience side effects, leading to treatment discontinuation⁵⁻⁷
 - Ongoing BCG shortages⁸
- Risks with radical cystectomy**
 - Post-operative complications^{9,10}
 - Impact on quality of life¹⁰



1. Sylvester RJ, et al. *Eur Urol* 2006; 49: 466. 2. Kamat AM, et al. *J Clin Oncol*. 2016;34(16):1935-44. doi: 10.1200/JCO.2015.64.4070. Epub 2016 Jan 25. 3. Roumiguie M, et al. *Eur Urol* 2022; 82:34-46. 4. Longoni M, et al. *Eur Urol Oncol*. 2025; 8: S2588-9311(25)00081-1. 5. Brausi M, et al. *Eur Urol*. 2014; 65(1):69-76. 6. Tapiero S, et al. *Urology*. 2018; 118: 107-113. 7. Van Der Meijden, et al. *Eur Urol*. 2003; 44(4): 429-434. 8. Holzbeierlein J, et al. *J Urol*. 2024;10.1097/JU.0000000000003846. 9. Maibom SL, et al. *BMJ Open*. 2021 Apr 14;11(4):e043266. doi: 10.1136/bmjopen-2020-043266. 10. Clements M, et al. *Eur Urol*. 2021;81(3), 294-304. <https://doi.org/10.1016/j.eururo.2021.09.018>.

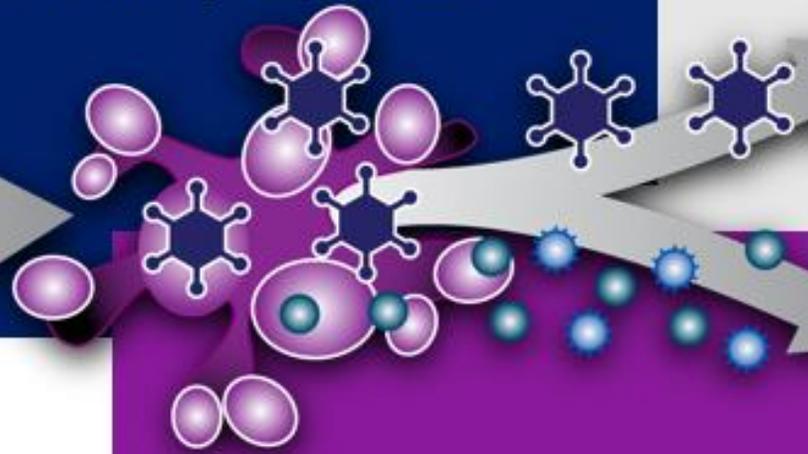
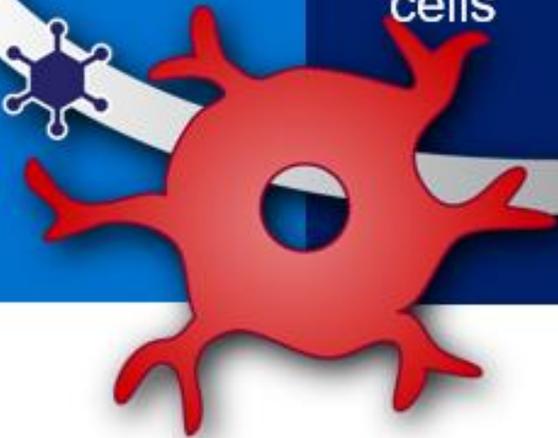


Oncolytic Immunotherapy: Cretostimogene Grenadenorepvec's Dual Mechanism of Action

- 1 Selectively Replicates in and Lyses Bladder Cancer Cells

Enters target cell

Replicates in and lyses cancer cells

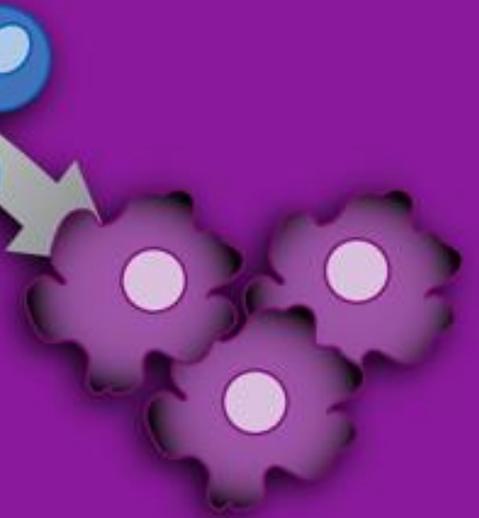


Chain Reaction of Cancer Cell Death:
Viral progeny spread to additional
tumor cells

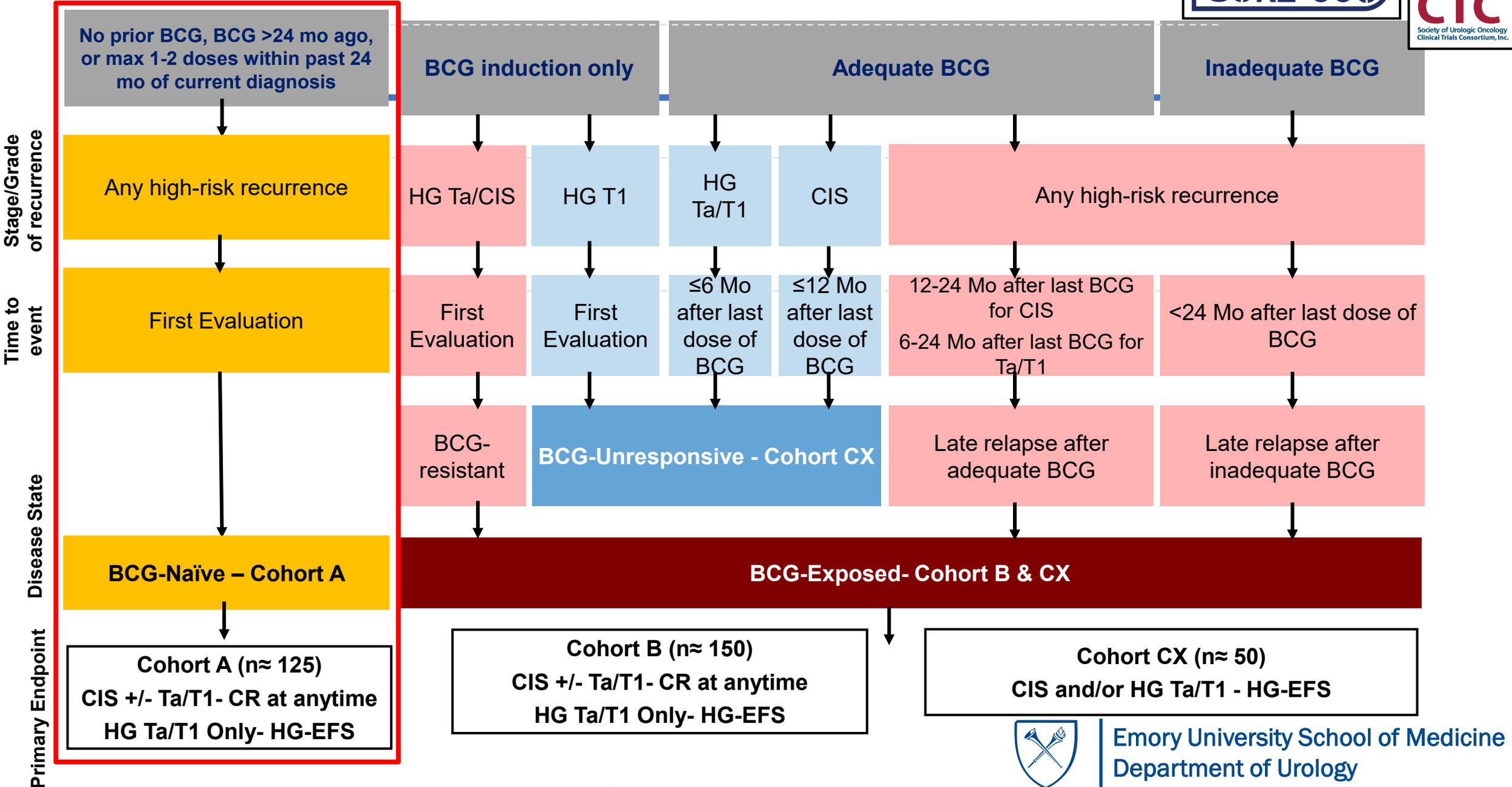
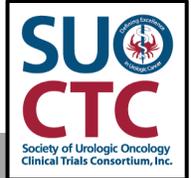


- 2 Simultaneously Amplifies Anti-tumor Immune Response

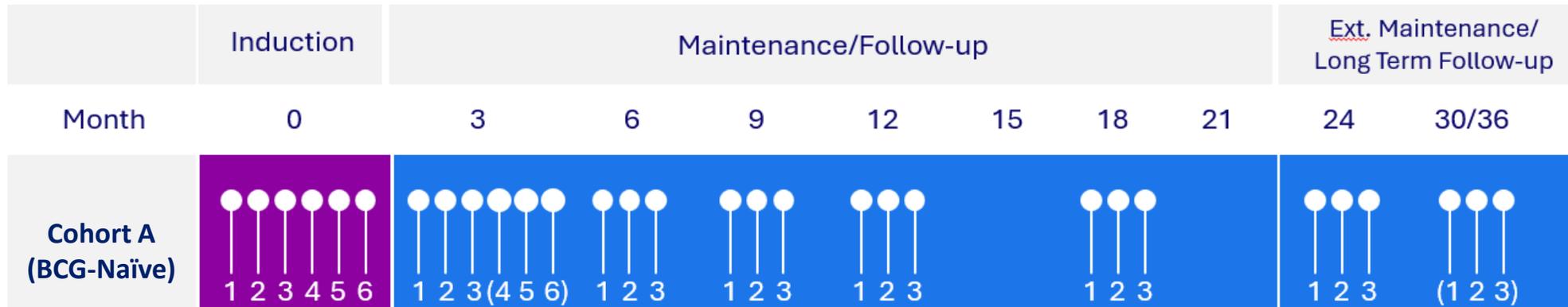
Innate to Adaptive Immune Switch:
Cytokine and antigen release
activates T & B-cells, inducing
immunologic memory



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



Treatment & Assessment Schedule



- Re-induction allowed for patients with HG Ta and/or CIS at Month 3
- Randomized 1:1 (Original 5-step [Arm 1] or Optimized 2-step [Arm 2] instillation)
- Cystoscopy & Cytology every 3 months with biopsies as clinically indicated at 12 Mo
- CT/MRU every 6 months
- Treatment is optional in Year 3



Patient Demographics & Baseline Characteristics

Patients in Safety Dataset	N=54	%
Gender		
Male	49	90.7
Female	5	9.3
Age (Years)		
Mean (SD)	73.2 (8.84)	
Median (Range)	73.5 (69-79)	
Age (Categories)		
< 65	6	11.1
≥ 65 and < 75	22	40.7
≥75	26	48.1
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

- Majority of patients are:
 - Male (90.7%)
 - White (92.6%)
 - > 65 years (88.8%)
- All patients enrolled from the U.S.



Patient Demographics & Baseline Characteristics

Patients in Safety Dataset	CIS Overall (N=54)	Original Admin* (N=27)	Optimized Admin** (N=27)
Gender			
Male	49 (90.7%)	23 (85.2%)	26 (96.3%)
Female	5 (9.3%)	4 (14.8%)	1 (3.7%)
Age (Years)			
Mean (SD)	73.2 (8.84)	72.9 (9.93)	73.4 (7.78)
Median (Range)	73.5 (40-87)	73.0 (40-87)	74.0 (57-87)
Age (Categories)			
< 65	6 (11.1%)	2 (7.4%)	4 (14.8%)
≥ 65 and < 75	22 (40.7%)	12 (44.4%)	10 (37.0%)
≥75	26 (48.1%)	13 (48.1%)	13 (48.1%)
ECOG PS			
ECOG PS 0	44 (81.5%)	25 (92.6%)	19 (70.4%)
ECOG PS 1	10 (18.5%)	2 (7.4%)	8 (29.6%)
HR NMIBC T-Stage at Study Entry			
CIS alone	24 (44.4%)	13 (48.1%)	11 (40.7%)
CIS with HG Ta	17 (31.5%)	11 (40.7%)	6 (22.2%)
CIS with HG T1	13 (24.1%)	3 (11.1%)	10 (37.0%)
BCG History, n (%)			
No Prior BCG	47 (87.0%)	22 (81.5%)	25 (92.6%)
BCG >24 Mo Ago	7 (13.0%)	5 (18.5%)	2 (7.4%)
Prior Adjuvant IVE Chemotherapy, n (%)			
Adjuvant IVE Chemotherapy	7 (13.0%)	5 (18.5%)	2 (7.4%)
No Adjuvant IVE Chemotherapy	47 (87.0%)	22 (81.5%)	25 (92.6%)

- Well balanced cohort of high risk NMIBC in original vs optimized administration approaches.

* Original administration included 5-step instillation with series of bladder saline washes followed by DDM and cretostimogene instillations
 ** Optimized administration streamlined the process to 2-steps inclusive of DDM followed by cretostimogene instillations

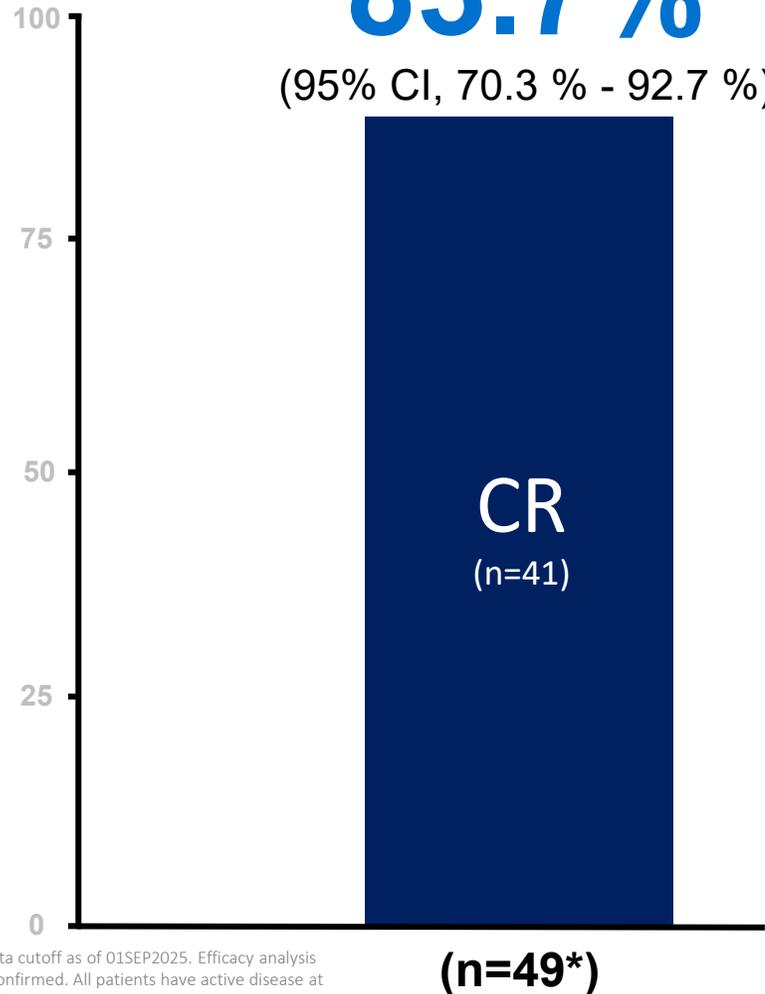


High Initial Response Rates from CORE-008 Cohort A

Complete Response at Anytime

83.7%

(95% CI, 70.3 % - 92.7 %)



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

- 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

* 49 patients were assessed for efficacy at the time of data cutoff. 4 re-induced patients are pending 6-month assessments.

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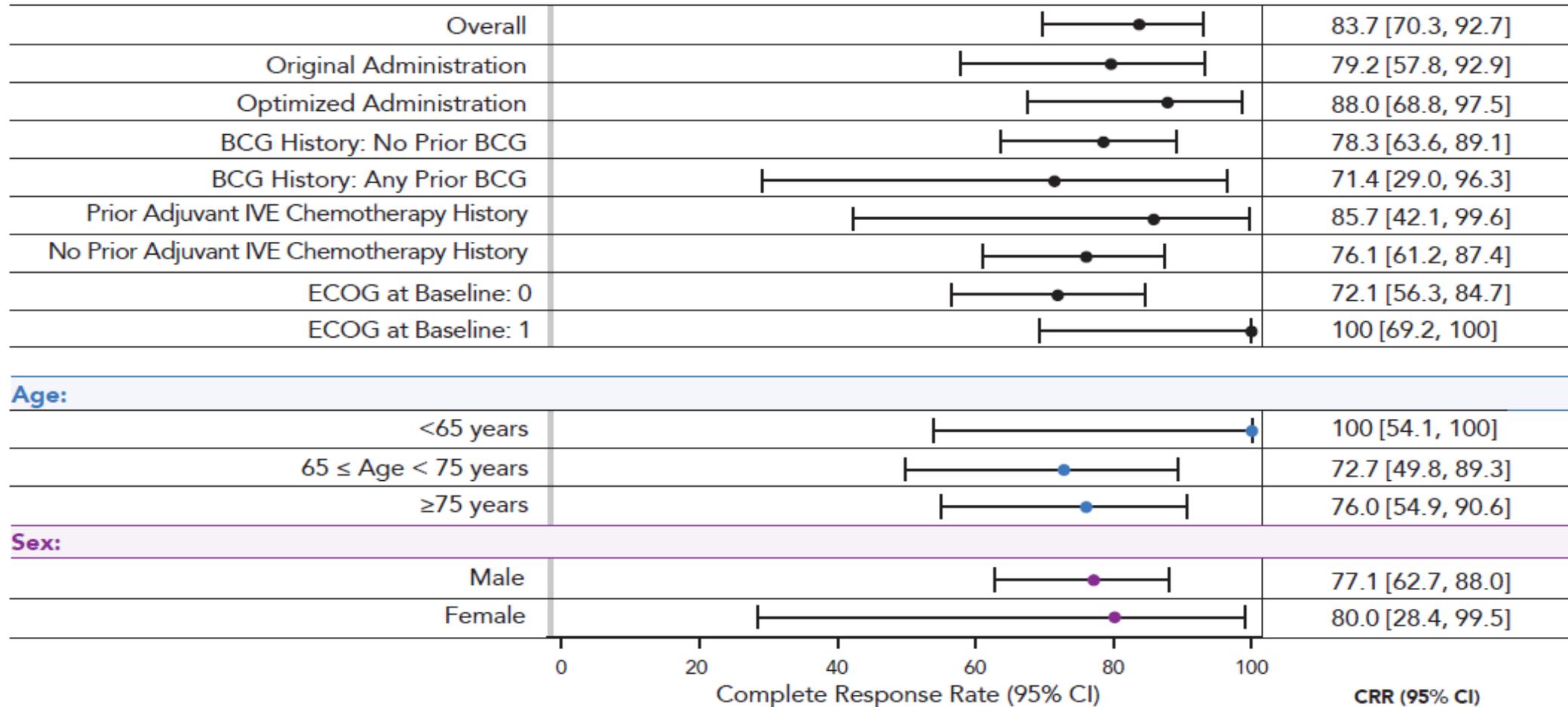
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A CR is defined as having a negative cystoscopy, a negative urine cytology, and a negative biopsy (as indicated). Analysis based on both landmark CR rate assessed in clinical trial and DoR by Kaplan-Meier estimate.



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Consistent Treatment-Effect Across Patient Subgroups



Favorable and Well-Tolerated Safety Profile

Preferred Term (MedDRA v.26.1)	CIS Overall (n=54)		Original Admin* (n=27)		Optimized Admin** (n=27)	
	Any Grade (%)	Grade ≥ 3	Any Grade (%)	Grade ≥ 3	Any Grade (%)	Grade ≥ 3
Patients with ≥ 1 TRAE	29 (53.7 %)	0 (0)	16 (59.3 %)	0 (0)	13 (48.1 %)	0 (0)
Treatment-Emergent AE reported in > 10% patients						
Bladder Spasm	13 (24.1 %)	0 (0)	8 (29.6 %)	0 (0)	5 (18.5 %)	0 (0)
Dysuria	11 (20.4 %)	0 (0)	7 (25.9 %)	0 (0)	4 (14.8 %)	0 (0)
Pollakiuria	8 (14.8 %)	0 (0)	5 (18.5 %)	0 (0)	3 (11.1 %)	0 (0)
Hematuria	8 (14.8 %)	0 (0)	3 (11.1 %)	0 (0)	5 (18.5 %)	0 (0)
Fatigue	8 (14.8 %)	0 (0)	1 (3.7 %)	0 (0)	7 (25.9 %)	0 (0)

- 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)

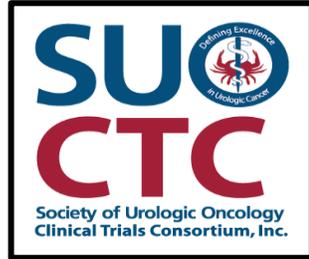


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CORE-008 Cohort A: Conclusions

- Cretostimogene monotherapy demonstrates **consistent efficacy, safety, and tolerability in HR BCG-Naïve NMIBC with CIS**
- Aligned with current urology workflows: intravesical, bladder-sparing, no systemic toxicities
- Flexibility permitted with **optimized administration**
- Findings support continued development of cretostimogene across NMIBC disease states
- **Additional treatment arms are planned for HR BCG-Naïve NMIBC**





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Thank You

All Bladder Cancer Patients and Their Families
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