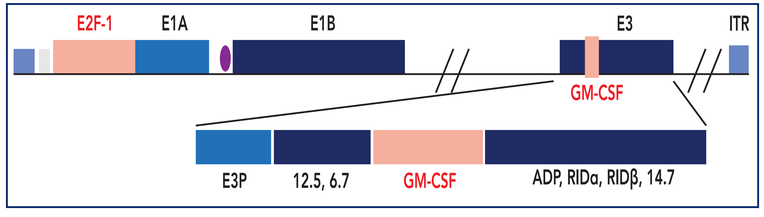
CORE-008: A Phase-2, Multi-Arm, Multi-Cohort, Open-Label Study of Cretostimogene Grenadenorepvec for the Treatment of High-Risk NMIBC

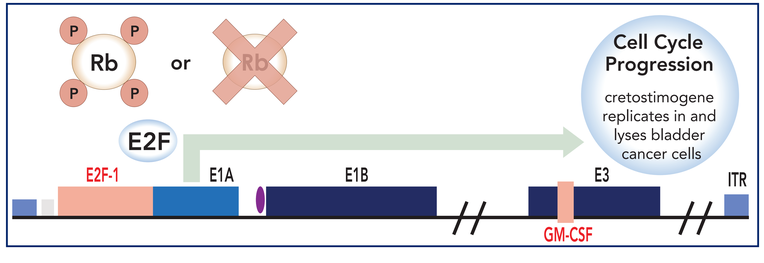
Trinity J. Bivalacqua, MD, PhD,[1] Siamak Daneshmand, MD,[2] Neal D. Shore, MD,[3] Shreyas S. Joshi, MD,[4] and Colin P. Dinney, MD [5]

[1] University of Pennsylvania, Philadelphia, Pennsylvania, [2] University of Southern California/Norris Comprehensive Cancer Center, Los Angeles, California, [3] Carolina Urologic Research Center, Myrtle Beach, South Carolina, [4] Emory University School of Medicine, Atlanta, Georgia, [5] University of Texas MD Anderson Cancer Center, Houston, Texas

BACKGROUND

- HR NMIBC challenges: considerable recurrence and progression risk; ongoing BCG shortage[1-2]
- Cretostimogene grenadenorepvec is an oncolytic immunotherapy with a dual mechanism of action
- Selectively replicates in and lyses cancer cells while simultaneously amplifying the immune response against bladder tumors
- Cretostimogene demonstrates Complete Response rates of 46-85% with favorable safety and tolerability in High-Risk NMIBC previously treated with BCG [3-8]
- Granted US FDA Fast Track and breakthrough Therapy Designations in HR BCG-UR NMIBC CIS +/- Ta/T1





CORE-008

SUO-CTC Sponsored

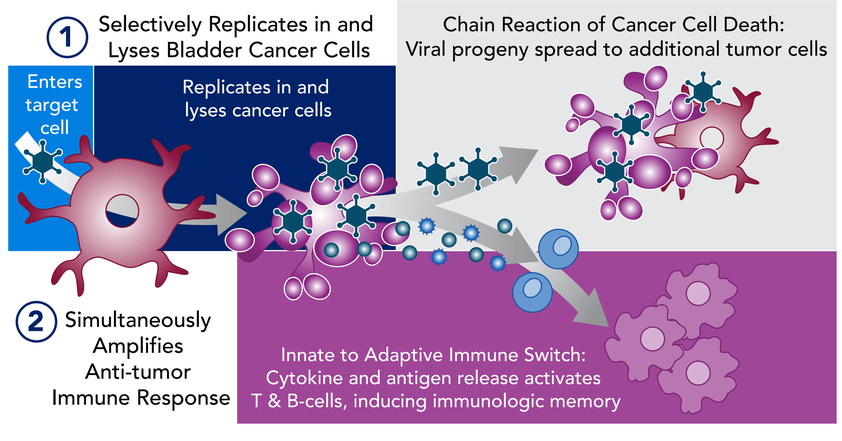
Trial in Progress

Actively Enrolling

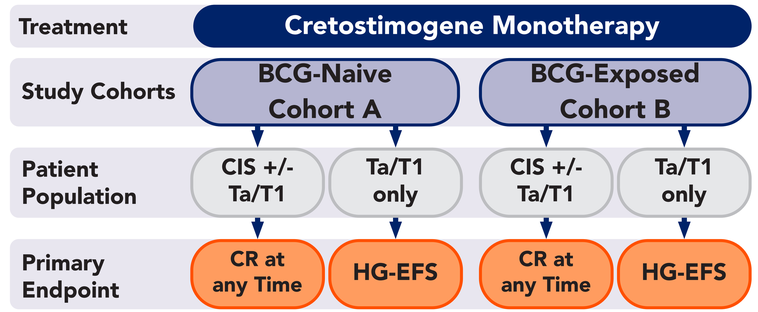
SUO CTC Society of Urologic Oncology Clinical Trials Consortium, Inc.

BCAN Bladder Cancer Advocacy Network

Oncolytic Immunotherapy: Cretostimogene Grenadenorepvec's Dual Mechanism of Action

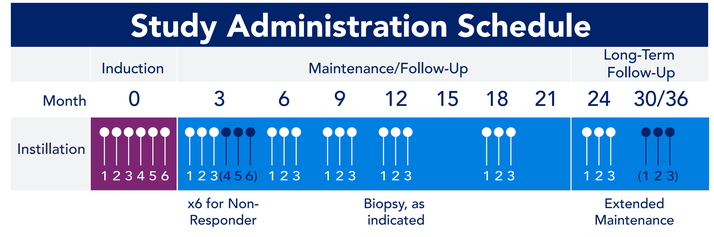


STUDY DESIGN



- High-Risk eligibility per AUA guidelines
- Secondary endpoints: DoR, all-cause EFS, CFS, safety
- Robust patient reported outcomes and biomarkers
- Additional cohorts forthcoming

Study Administration Schedule



Response Assessments include cystoscopy, biopsy as indicated & cytology every 3 months for first 2 years and every 6 months starting Year 3

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Contact Information:
Trinity J. Bivalacqua;
Trinity.Bivalacqua@pennmedicine.upenn.edu

References: **1** NCCN Bladder Cancer Guidelines; 2024, **2** AUA NMIBC Guidelines; 2024, **3** Burke, *J Urol*; 2012, **4** Packiam, *Uro Onc*; 2018, **5** Tyson, SUO meeting, 2024, **6** Li, *Nat Med*; 2024 **7** Tyson, SUO Meeting; 2023, **8** Tyson, AUA Meeting, 2024

ASCO® Genitourinary Cancers Symposium

CORE-008- A Phase 2, Multi-Arm, Multi-Cohort, Open-Label Study to Evaluate Intravesical Cretostimogene Grenadenorepvec in Participants with High-Risk Non-Muscle Invasive Bladder Cancer

Trinity J. Bivalacqua, MD PhD; Siamak Daneshmand, MD; Neal D. Shore, MD; Shreyas S. Joshi, MD and Colin P. Dinney, MD

Trinity Bivalacqua, MD, PhD

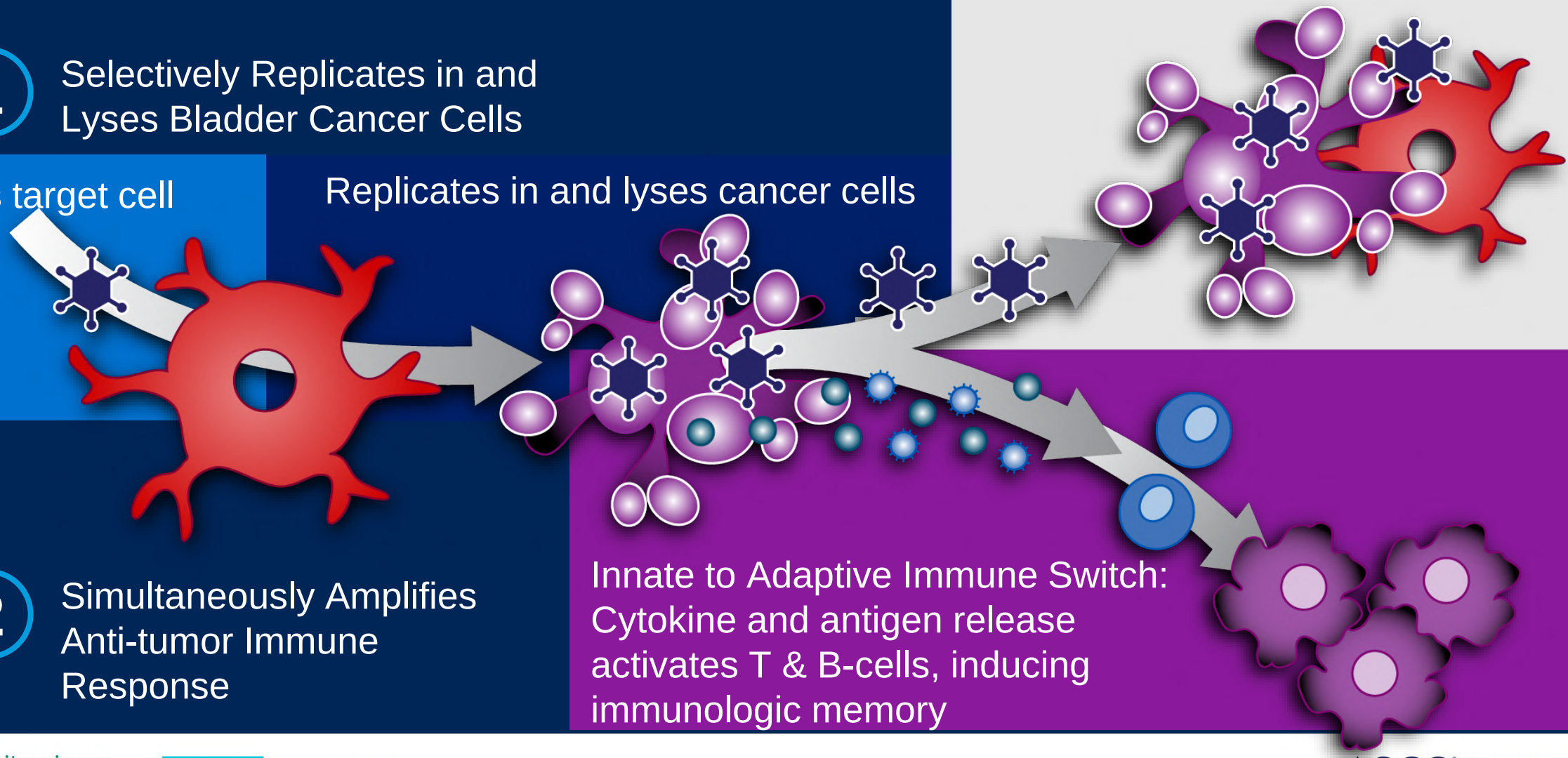
Oncolytic Immunotherapy: Cretostimogene Grenadenorepvec's Dual Mechanism of Action

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

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Phase 2, Multi-Cohort, Open-Label Study of Cretostimogene Grenadenorepvec in High-Risk NMIBC

High-Risk NMIBC

Cretostimogene Grenadenorepvec
Cohort A (BCG-naïve), Cohort B (BCG-exposed)

Primary Endpoint:
CR (CIS) or HG-EFS (Papillary)

Population / Key Entry Criteria

- AUA definition HR NMIBC
- BCG-naïve* (Cohort A)
- BCG-exposed** (Cohort B)
- Complete resection at baseline
- Adequate organ function
- ECOG 0-2

Study Design / Regimen

- Both Cohorts enrolling patients with CIS-containing and HG Ta/T1 only disease
- IVE Treatment Schedule
  - Induction course = Weekly x 6
  - Maintenance courses = Weekly x 3
- Disease assessment
  - Every 3 months cystoscopy and urine cytology for 2 years; then every 6 months in Years 3-4

Additional Endpoints

- DoR
- EFS and RFS
- Cystectomy-free survival
- Safety
- Exploratory endpoints include Biomarkers, HRQoL, PRO, OS

* BCG-naïve includes no prior treatment with BCG, no BCG within past 24 mo prior to current diagnosis, or maximum 1-2 doses of BCG within past 24 mo prior to current diagnosis
** BCG exposed includes BCG resistant and delayed relapse after adequate and inadequate BCG

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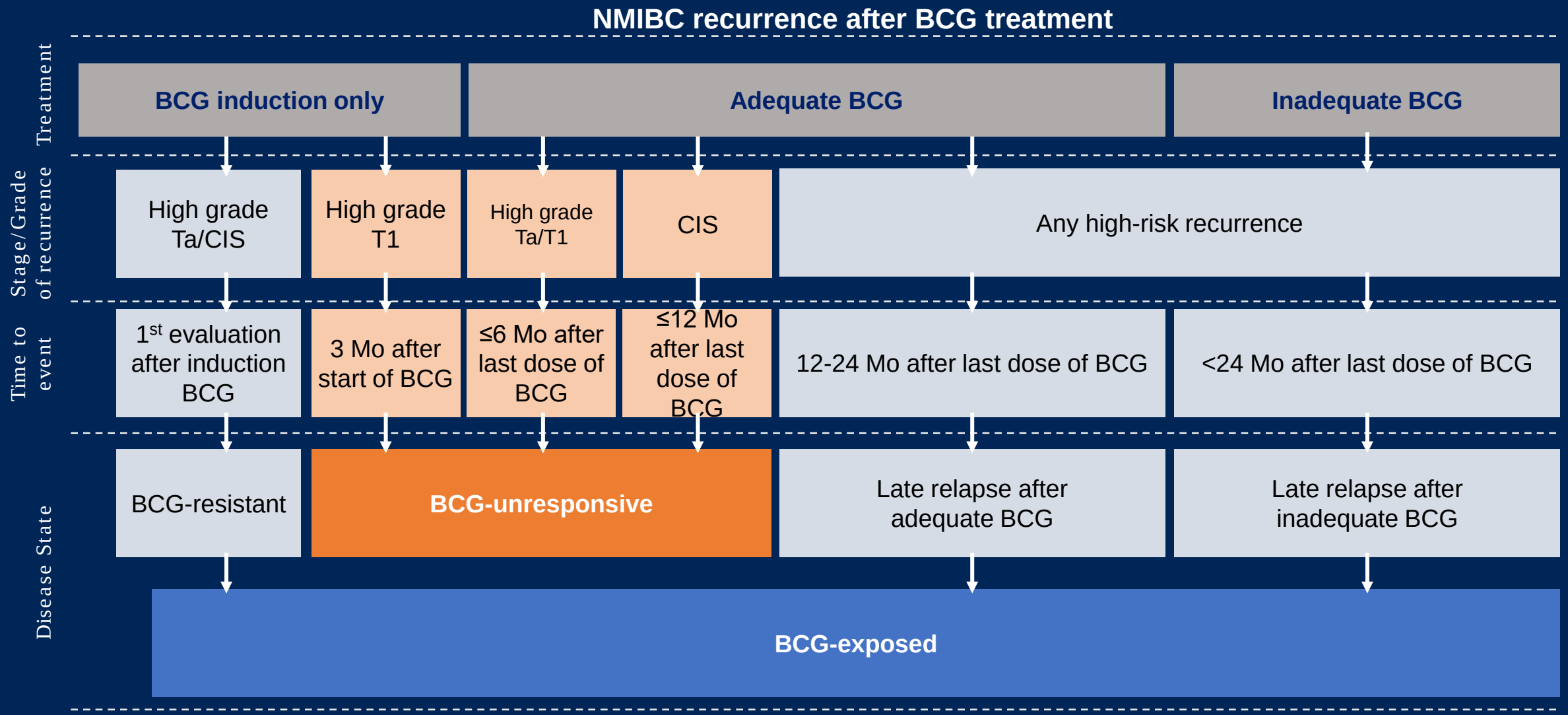
Pathological Inclusion Criteria



Roumiguié M, Kamat AM, Bivalacqua TJ, et al. Eur Urol. 2022 Jul;82(1):34-46. doi: 10.1016/j.eururo.2021.12.005. Epub 2021 Dec 23.

Treatment & Assessment Schedule

- Cystoscopy & Cytology every 3 months
- Mandatory biopsy at week 51
- CT/MRU every 6 months
- Re-induction allowed for patients with HG Ta and/or CIS at Month 3
- Treatment is optional in Year 3

Key Takeaways

- CORE-008 is a phase 2, multi-arm, multi-cohort trial evaluating cretostimogene in patients with HR NMIBC who are BCG-naïve or BCG-exposed
- Cretostimogene is an oncolytic immunotherapy with dual MOA
  - Postulated innate to adaptive immune switching
- Potentially effective, well tolerated, and durable regimen
- Easily fits within existing clinic workflow
- Future cohorts within HR NMIBC forthcoming