MAYO CLINIC

Pivotal Results from BOND-003: A Phase-3, Study of Intravesical Cretostimogene Grenadenorepvec for the Treatment of BCG-Unresponsive, High-Risk, NMIBC with CIS

P2 Plenary: Practice-changing, Paradigm-shifting Clinical Trial in Urology

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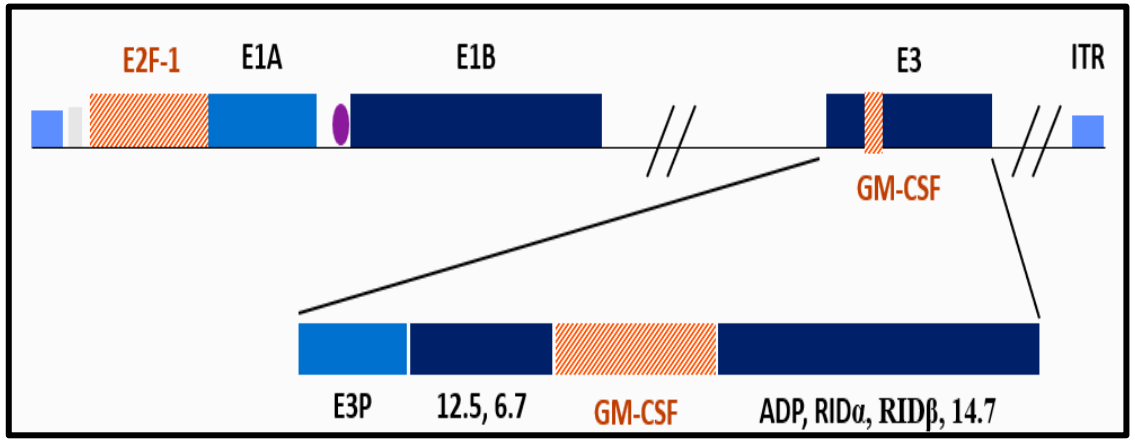
https://cgoncology.com/wp-content/uploads/2024/05/AUA 2024 Tyson_BOND-003_Plenary Presentation Final.pdf

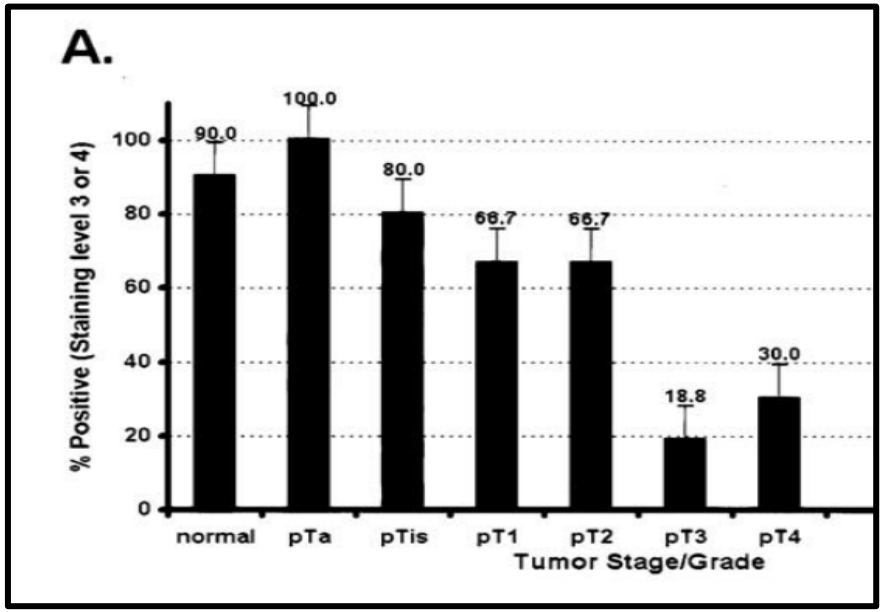
Disclosures

- CG Oncology- No Conflicts of Interest

What is Cretostimogene Grenadenorepvec?

- Conditionally replicating adenovirus
  - Highly immunogenic
- Oncolytic immunotherapy
  - Encodes GM-CSF
  - Insertion of human E2F-1 promoter
- Binds to Coxsackie Adenovirus Receptor (CAR)
  - Robust expression in all stages of bladder cancer
- Viral replication results in tumor lysis





CG Oncology proprietary illustration. Sachs, et al. Urology 2002
Burke, et al J Urol 2012

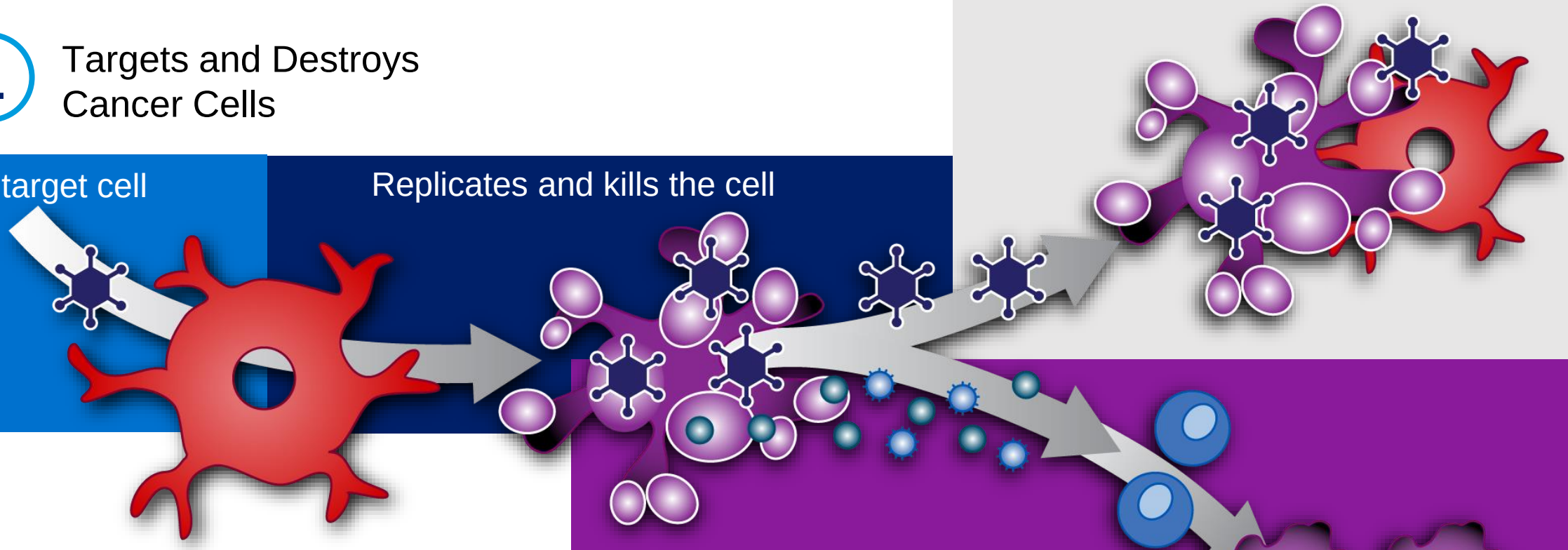
Oncolytic Immunotherapy: Selective Oncolysis and Potent Anti-Tumor Immune Response

1 Targets and Destroys Cancer Cells

Enters target cell

Replicates and kills the cell

Spreads to additional tumor cells inducing a chain reaction of further cancer cell death



2 Stimulation of Anti-tumor Immune Response

Virus stimulates cytokines and antigens from dying cancer cells which activates T-cells inducing tumor cell death and destruction

BOND-003: Phase-3 Single Arm, BCG-UR NMIBC with CIS

Cohort C Population (N=112):

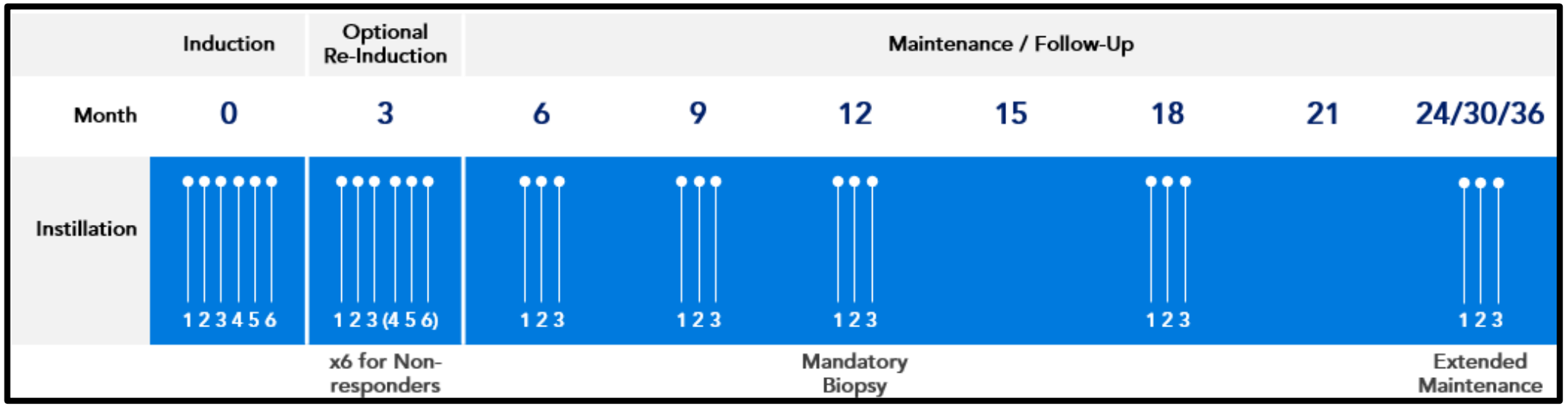
- Age ≥ 18 yo
- ECOG PS 0-2
- Pathologically confirmed BCG-UR HR NMIBC <u>with CIS</u> +/- papillary disease

Primary Endpoint:

- CR at any time

Secondary Endpoints:

- Duration of Response
- CFS, PFS, RFS



Response Assessments: Cystoscopy, biopsy as indicated, and cytology Q3M X 2 years and Q6M starting Year 3

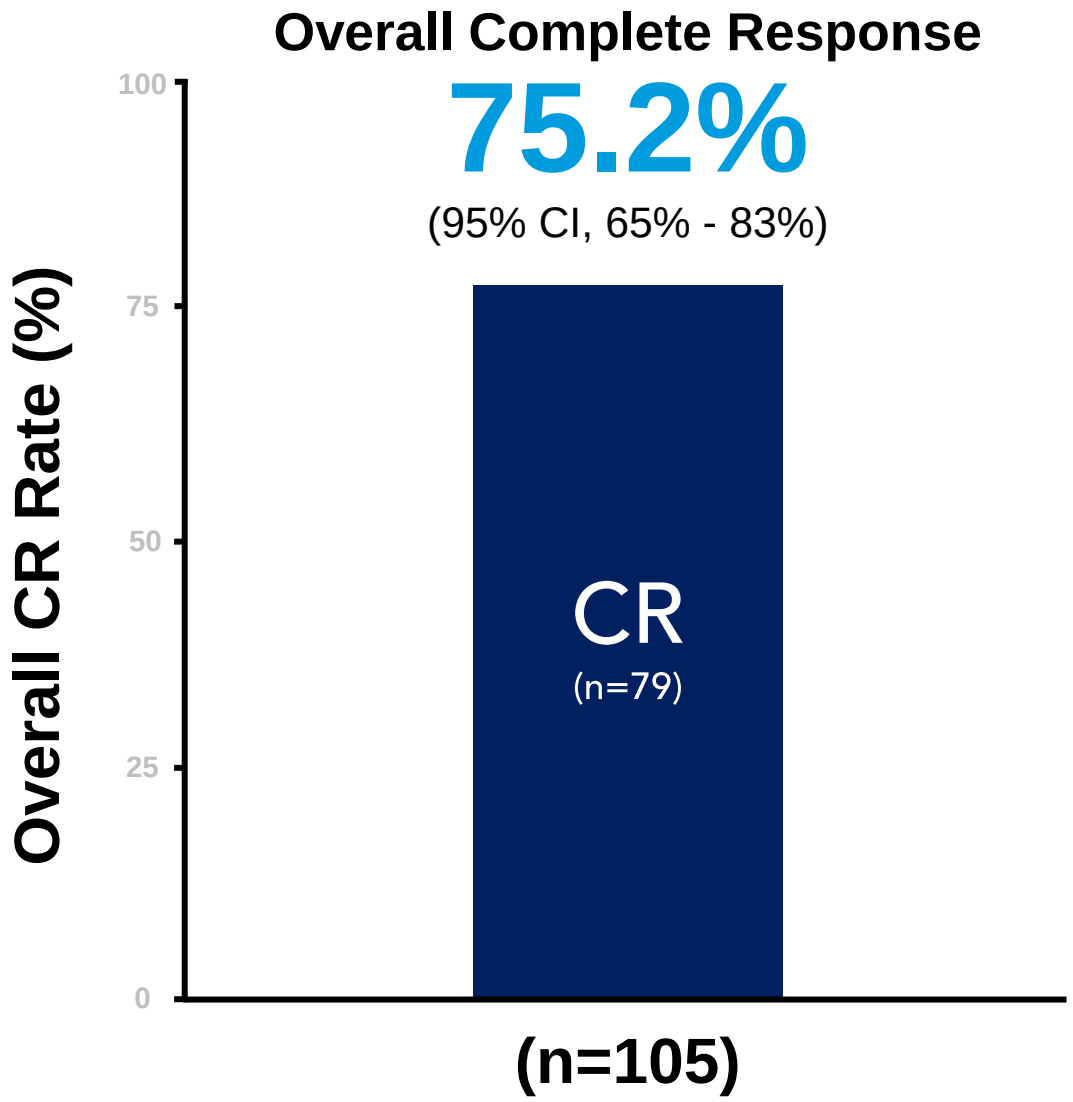
BOND-003: Patient Demographics (Cohort C)

Subjects in Efficacy Dataset	N=112	%
Gender		
Male	83	74.1
Female	29	25.9
Age (Years)		
Mean (SD)	72.9 (9.19)	
Median (Range)	74.0 (43-90)	
Age (Categories)		
< 65	19	17.0
> 65	93	83.0
BCG History: Number of Prior Instillations		
Median (Range)	12 (7 – 66)	
High-Risk NMIBC T-Stage at Study Entry		
CIS with T1	6	5.3
CIS with Ta HG	16	14.3
CIS	90	80.4

- Majority of patients are:
  - Male (74%)
  - White (61%)
  - > 65 years (83%)
- Highly pre-treated population
  - Includes patients with prior intravesical chemotherapy and systemic immunotherapy

Efficacy data cutoff as of 01APR2024.

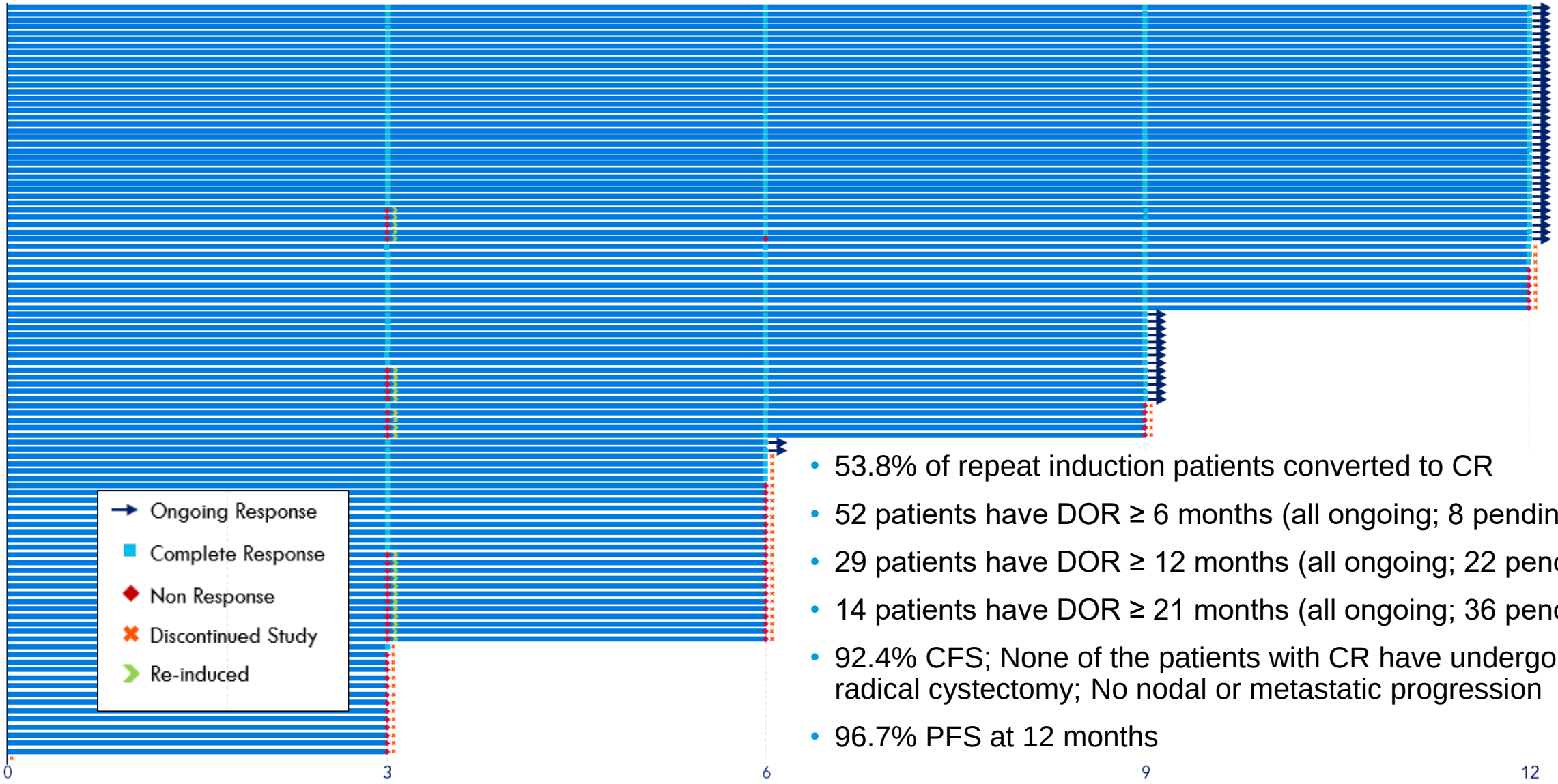
Cretostimogene Monotherapy Results: 75.2% CR at Any Time



Efficacy data cutoff as of 01APR2024

Efficacy analysis centrally confirmed. All pts have active disease at baseline prior to enrollment. Received adequate BCG per FDA 2018 guidance

Cretostimogene Has Shown Durable Responses Over Time



- 53.8% of repeat induction patients converted to CR
- 52 patients have DOR ≥ 6 months (all ongoing; 8 pending)
- 29 patients have DOR ≥ 12 months (all ongoing; 22 pending)
- 14 patients have DOR ≥ 21 months (all ongoing; 36 pending)
- 92.4% CFS; None of the patients with CR have undergone radical cystectomy; No nodal or metastatic progression
- 96.7% PFS at 12 months

Efficacy data cutoff as of 01APR2024.

Cretostimogene Has Been Generally Well-Tolerated

Preferred Term (MedDRA v.26.1)	Cretostimogene (n=112)	
	Any Grade (%)	Grade ≥ 3
Patients with ≥ 1 TRAE	70 (62.5%)	0 (0)
Treatment-Related AE reported in > 10% patients		
Bladder Spasm	26 (23.2%)	0 (0)
Pollakiuria	22 (19.6%)	0 (0)
Dysuria	17 (15.2%)	0 (0)
Micturition Urgency	17 (15.2%)	0 (0)
Hematuria	16 (14.2%)	0 (0)

- Most AEs were Grade 1-2
- No grade ≥ 3 treatment-related AEs or deaths reported
- 2 patients (1.8%) had serious treatment-related AEs (Grade 2)*
- 1 patient discontinued treatment due to unrelated AE**
- 94.5% completed all expected treatments

Safety data cutoff as of 31JAN2024
* Treatment-related SAEs were Cystitis noninfective (Grade 2) and clot retention (Grade 2).
** Unrelated AE leading to treatment discontinuation was Hematuria (Grade 2).

Experience with Cretostimogene

- Familiar and convenient instillation process/schedule for practices
  - Thaw time up to 10 minutes
- Administered by allied healthcare professionals (MAs, RNs)
- Generally well-tolerated regimen
- 100% of patients with successful instillation on BOND-003
- Streamlined instillation process for future cohorts and studies

Cretostimogene Has Potential to Become Backbone Therapy in NMIBC Treatment Landscape[1]

Trial	BOND-003	CORE-001[2]	QUILT 3.032	NCT02773849	KEYNOTE-057
Intervention	**Cretostimogene**	**Cretostimogene + Pembrolizumab**	N-803 + BCG	Nadofaragene	Pembrolizumab
Mechanism	Oncolytic Immunotherapy	Oncolytic Immunotherapy + Checkpoint Inhibitor	IL-15 Superagonist + BCG	Gene Therapy Secreting IFN	Checkpoint Inhibitor
RoA	Intravesical	Intravesical + Intravenous	Intravesical	Intravesical	Intravenous
Stage	Phase 3 Enrollment Complete	Phase 2 Ongoing	Approved April 22, 2024	Approved	Approved
Sample Size	N=112	N=35	N=77	N=98	N=96
CR Any Time	**75% (79/105)***	85% (29/34)*	62% (48/77)	51% (50/98)	41% (39/96)
DOR ≥ 12 Mo	**83% (29/35)***	88% (14/16)*	58% (28/48)	46% (23/50)	46% (18/39)
Safety Profile	0% Grade 3 TRAE 0% Grade 4 TRAE **0% treatment-related discontinuation**	Creto-related: 0% Grade 3 TRAE **4 pembro-related discontinuation of pembrolizumab[2]**	**16% SAE**, including fatal adverse reaction of cardiac arrest in one patient on treatment; **7% treatment-related discontinuation[3]**	4% Grade 3+ TRAE **3% treatment-related discontinuation[4]**	11% Grade 3 TRAE 2% Grade 4 TRAE **11% treatment-related discontinuation[5]**

* Pending additional assessment and evaluation at subsequent timepoints

1. Not based on head-to-head or comparator studies. Differences exist between trial designs and participants; caution should be exercised when comparing these data 2. Interim efficacy data (03MAR2023) and safety data (31JAN2024) at AUA 2023; 3. ANKTIVA® Package Insert; 4. ADSTILADRIN® Package Insert and Boorjian, Lancet Oncol. 2021 5. KEYTRUDA® Package Insert and Balar, Lancet Oncol. 2021

Fast Track & Breakthrough Therapy Designations Granted for Cretostimogene Monotherapy in BCG-UR CIS +/- Papillary Disease!

FDA
Breakthrough Therapy Designation

FDA
Fast Track Designation

Next Phase of BOND-003 Trial (Cohort P)

Trial Extension & Addition of BCG-UR Papillary Only Cohort

Treatment Extension

Maintenance Extension:
Complete Responders eligible for maintenance through Year 3

Maintenance Dosing:
Weekly x 3 Q3M in Year 1
Weekly x 3 Q6M in Year 2 and Year 3

Addition of Papillary Cohort (n~75)

Dosing Schedule:
Standard Cretostimogene induction and maintenance schedule

Summary of Changes:
Patients will have the option for repeat induction, if in non-response at 3 Months

BOND-003 COHORT C

Visit the AUA Learning Lab on <u>Sunday, May 05 @ 10:56 AM</u> for more information on BOND-003 Cohort P

BOND-003 COHORT P

Cretostimogene Expanded Access Program (EAP)

Program Objectives

- Available for a broader range of patients with CIS-containing BCG-UR NMIBC
- Prioritize geographically and ethnically diverse population of real-world patients
- CG Oncology will provide supply of cretostimogene

Dosing Regimen

Induction Course:
Weekly x 6

Second Induction:
Weekly x 6 for non-responders

Maintenance Course:
Weekly x 3 Q3M for Year 1
Weekly x 3 Q6M for Year 2

Data Collection

- Safety
- Efficacy
- PROs

CRETO-EAP
EXPANDED ACCESS PROGRAM

BCG-UR- Bacillus Calmette Guerin unresponsive; CIS- Carcinoma *in situ*; NMIBC- Non-Muscle Invasive Bladder Cancer; PRO-patient reported outcomes
*EAP includes expanded eligibility, BCG-UR

Further Steps: SUO-CTC Supported Clinical Trials

PIVOT-006: Phase-3 Adjuvant Cretostimogene Versus Surveillance in IR-NMIBC

- >90 sites participating
- Patients dosed!
- Dr. Robert Svatek Global PI
  - *AUA Learning Lab- May 5, 10:24 AM*

CORE-008: Phase-2 Multi-arm, Multi-cohort Cretostimogene in HR-NMIBC

- Cohort A: BCG-Naïve
- Cohort B: BCG-Exposed
- Additional cohorts under design

Acknowledgements

All Bladder Cancer Patients and Their Families

The Study Coordinators and Nurses

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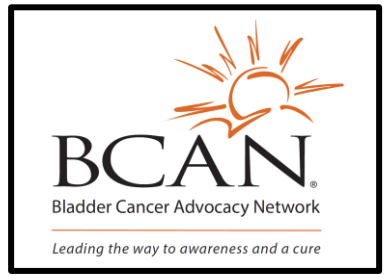

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THANK YOU!

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