MAYO CLINIC

BOND-003- Cohort P: A Multi-national, Single-arm Study of Intravesical Cretostimogene Grenadenorepvec for the Treatment of High Risk, Papillary Only, BCG-Unresponsive NMIBC

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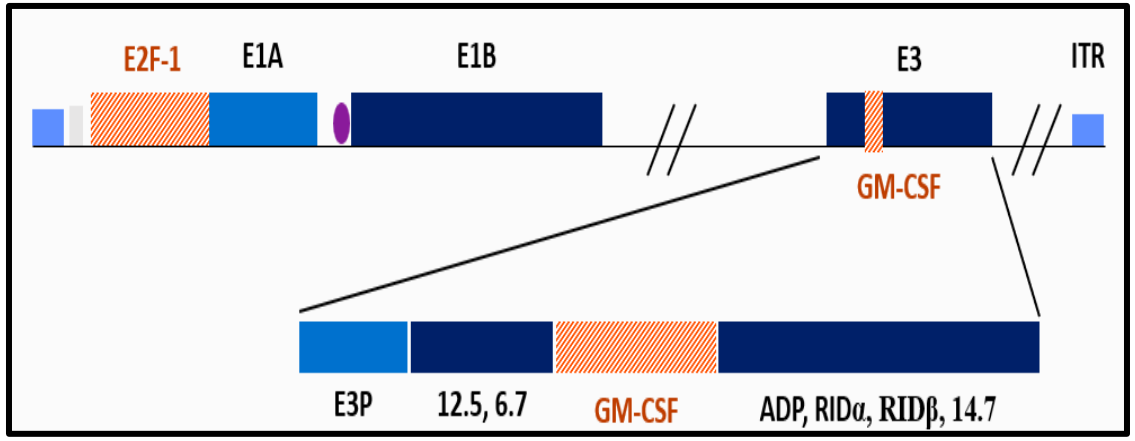
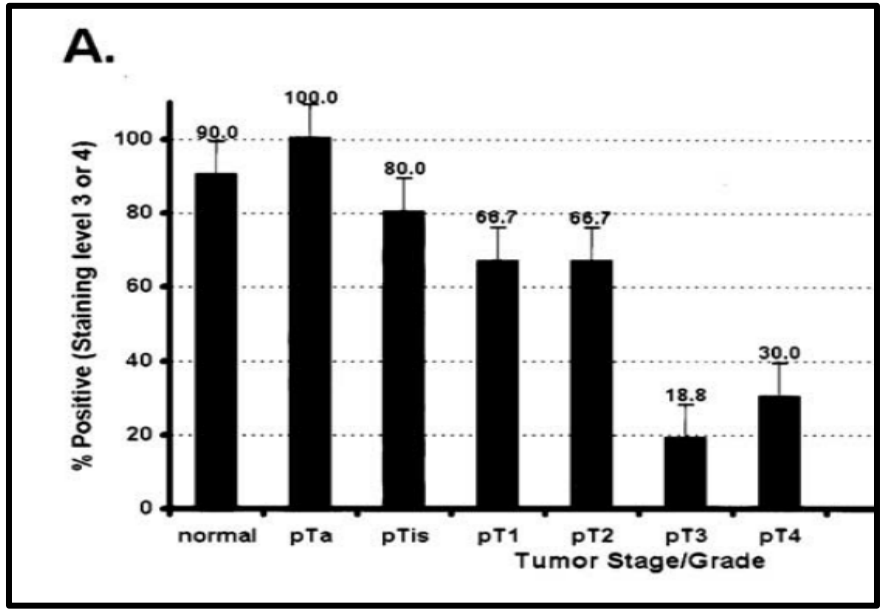
https://cgoncology.com/wp-content/uploads/2023/10/SUO_2023_First_Results_from_BOND-003.pdf

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

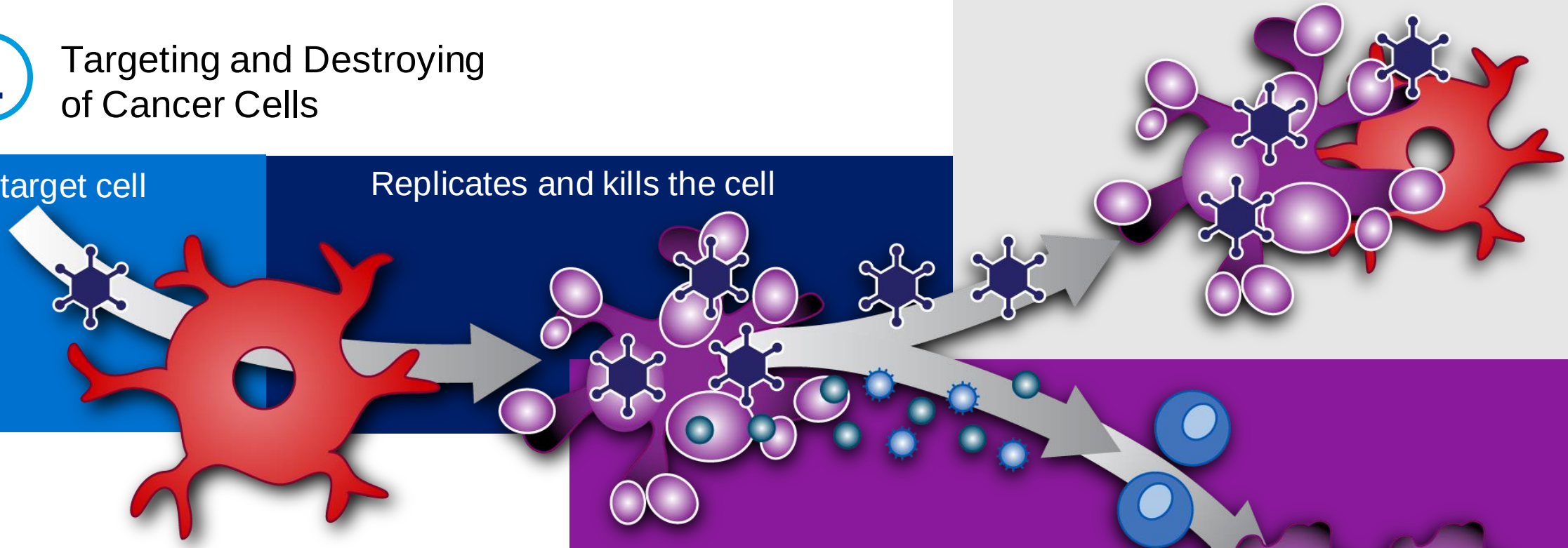
Oncolytic Immunotherapy: Selective Oncolysis and Potent Anti-Tumor Immune Response

1 Targeting and Destroying of Cancer Cells

Enters target cell

Replicates and kills the cell

Spreads to additional tumor cells inducing a chain reaction of killing cancer cells



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 Trial Cretostimogene Monotherapy for BCG-UR High-Risk NMIBC

(NCT04452591)

Study Design

BOND-003 : BCG-UR, High-Risk NMIBC

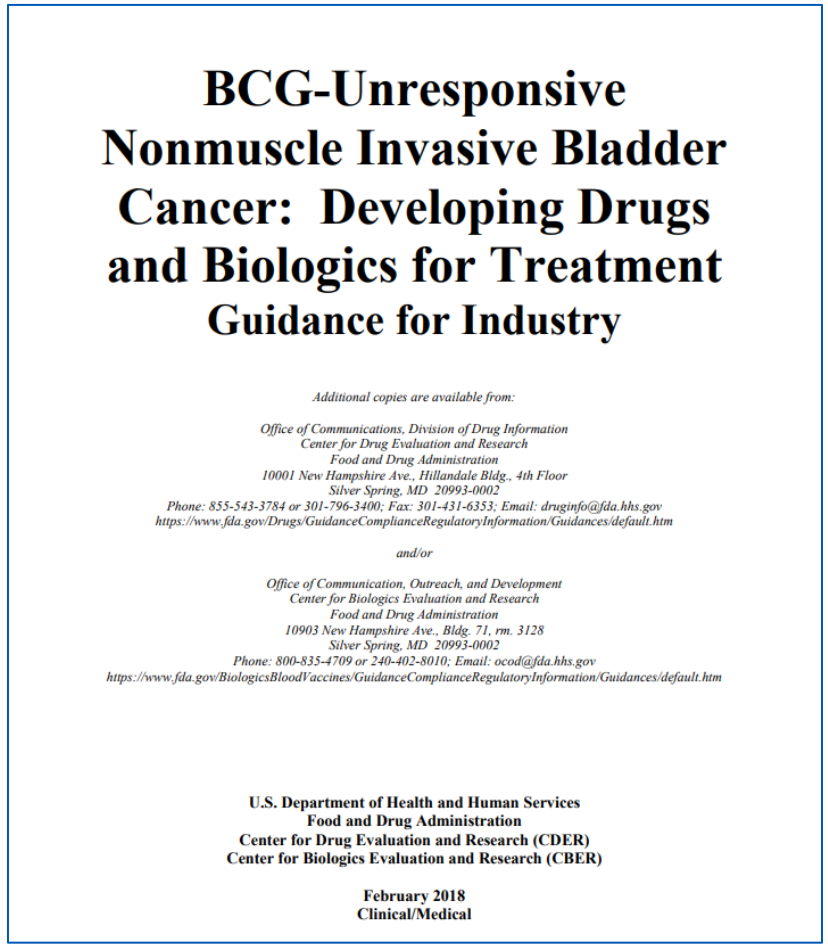
Cohort C
CIS +/- Ta/T1
(n=115)

Induction + Maintenance with Cretostimogene

Cohort P
Ta/T1 only
(N=70)

Primary Endpoint:
CR

Primary Endpoint:
EFS



BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment
Guidance for Industry

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353; Email: druginfo@fda.hhs.gov
https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

and/or

Office of Communication, Outreach, and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, rm. 3128
Silver Spring, MD 20993-0002
Phone: 800-835-4709 or 240-402-8010; Email: ocod@fda.hhs.gov
https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

February 2018
Clinical/Medical

CIS +/- Ta/T1- Carcinoma *in situ*, with or without Ta/T1; CR- Complete Response; EFS- Event Free Survival; NMIBC- Non-Muscle Invasive Bladder Cancer
FDA Guidance Document: BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment. February 2018 .

BCG-UR NMIBC STUDY DESIGN CONSIDERATIONS

Recommendations from 2018 FDA Guidance

- Single-arm trials are appropriate for studies including patients with BCG-UR NMIBC
- Primary efficacy endpoint(s):
  - CR in patients with CIS
  - Time-to-event endpoint for patients with completely resected Ta/T1 papillary disease
- Current FDA approved agents for BCG-UR may be considered for high-risk papillary Ta/T1 only tumors without CIS (NCCN®; category 2B)

CIS +/- Ta/T1- Carcinoma *in situ*, with or without Ta/T1; CR- Complete Response; NCCN-National Comprehensive Cancer Network; NMIBC- Non-Muscle Invasive Bladder Cancer
FDA Guidance Document: BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment. February 2018 .

INCLUDE COHORT C RESULTS?

- CR at any time
- DOR/HGRFS with CIS+papillary results reason for Cohort P
- Safety slide

Fast Track & Breakthrough Therapy Designation Granted for Cretostimogene Monotherapy in BCG-UR CIS +/- Ta/T1 Papillary Disease!

FDA
Breakthrough Therapy Designation

FDA
Fast Track Designation

SIGNIFICANT UNMET NEED PAPILLARY DISEASE

- Current options are FDA approved for BCG-UR CIS+/- Ta/T1 NMIBC
- A majority of BCG-UR patients present with high-risk Ta/T1 papillary disease without CIS (reference?)
- An unmet medical need exists for treatment options for high-risk Ta/T1 papillary disease

BCG- Bacillus Calmette Guerin; CIS +/- Ta/T1- Carcinoma *in situ*, with or without Ta/T1; NMIBC- Non-Muscle Invasive Bladder Cancer
FDA Guidance Document: BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment. February 2018 .

ELIGIBILITY CRITERIA

Inclusion Criteria

- Age ≥18 years
- ECOG performance status of 0-2
- Histologically confirmed BCG-UR HG Ta/T1 papillary disease without CIS within eight weeks of study enrollment
- BCG unresponsive defined per FDA guidance*
- Patients received adequate BCG by the US FDA definition
- Patients must have no evidence of residual bladder cancer before treatment
- recurrent HG Ta/T1 within 6 month of last adequate BCG dose. Patients who recur with HG T1 after a single induction course of BCG may be eligible

Exclusion Criteria

- Same as Cohort C

CIS +/- Ta/T1- Carcinoma *in situ*, with or without Ta/T1; CR- Complete Response; EFS- Event Free Survival; NMIBC- Non-Muscle Invasive Bladder Cancer; ECOG- Eastern Cooperative Oncology Group ;
FDA Guidance Document: BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment. February 2018 .

ENDPOINTS

Primary Endpoint

- High-grade Event Free Survival (EFS)

Secondary Endpoint(s)

- High- and low-grade Recurrence Free Survival (RFS)
- Progression Free Survival (PFS)
- All-cause EFS
- Radical Cystectomy Free Survival
- Bladder Cancer Specific Survival
- Safety & tolerability
- Time to next intervention

Exploratory Endpoint(s)

- Patient-reported quality of life
- Biomarker analyses
- Coxsackie adenovirus receptor and E2F promoter expression
- Neutralizing antibodies and markers of immunogenicity

Experience with Cretostimogene

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Project: CG Oncology
Date: 21-03-2024
Runtime projection: 150 sec
Stage: Animation
Version: 1.0
Comment: Full MoA version
Music: On
Sound effects: On
Voiceover: On (Studio)
On-screen text: On
Special effects: On
Materials and textures: On
Colour palette: Final
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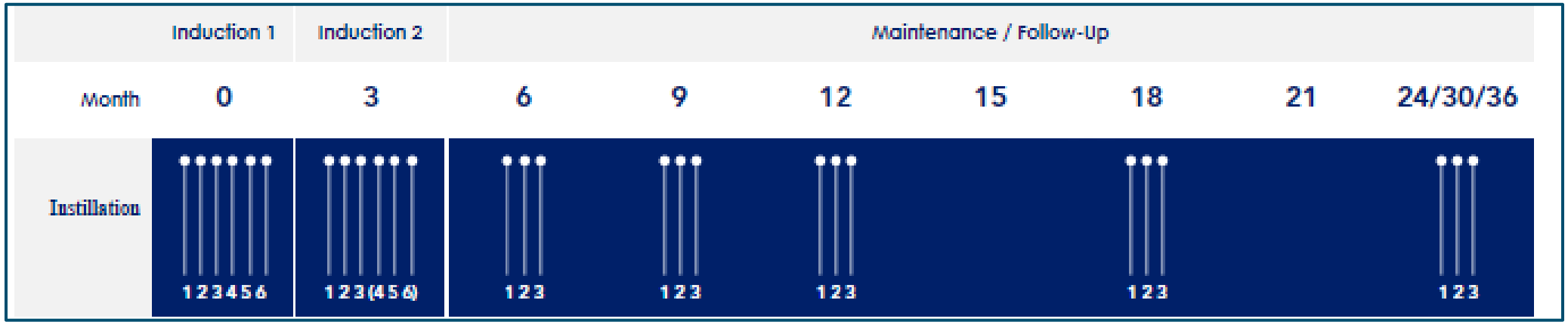
- Familiar and convenient administration process and schedule for urology practices
- Administered by allied healthcare professionals (MAs, RNs)
- Further streamlining instillation process for future studies



Response Assessment will include cystoscopy, biopsy as indicated, and cytology every 3 months for first 2 years and every 6 months starting Year 3. Mandatory bladder biopsies directed at prior tumor location(s) will be performed at month 12. Patients will have the option for repeat induction, if in response, then maintenance

BOND-003 COHORT P: TRIAL IN PROGRESS

- Patient identification, screening & selection are ongoing
- 35+ sites selected across US and Japan
- Add milestone timeline?

- Contact Information:
  - Mark Tyson, MD, MPH, BOND-003 Global PI,
  - Tyson.Mark@mayo.edu

Acknowledgements

All BCG-Unresponsive Bladder Cancer Patients and Their Families

The Study Coordinators and Nurses

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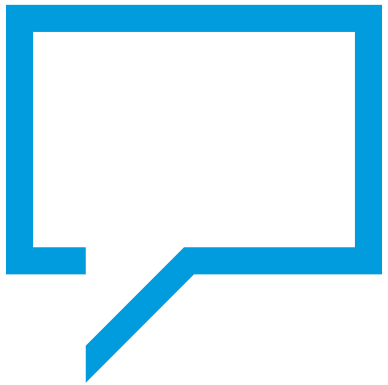
THANK YOU & QUESTIONS



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