Expanded Access Program of Cretostimogene Grenadenorepvec in Patients with High-Risk BCG-Unresponsive NMIBC with CIS

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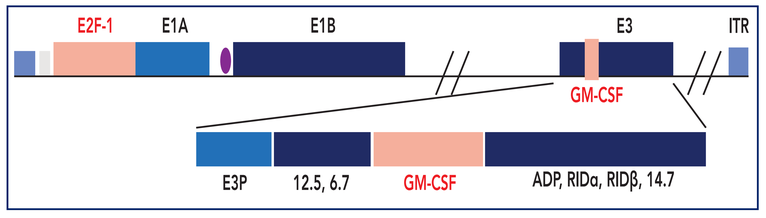
BACKGROUND

- Cretostimogene grenadenorepvec is an oncolytic immunotherapy with a dual mechanism of action: selectively replicates in and lyses cancer cells and 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 [1-7]
- Granted US FDA Fast Track and Breakthrough Therapy Designations in HR BCG-UR NMIBC CIS +/- Ta/T1
- CRETO-EAP will offer treatment for patients ineligible for, or have limited access to, other BCG-UR CIS clinical trials[8]



References: **1** Burke, J Urol; 2012, **2** Packiam, Uro Onc; 2018, **3** Li, AUA Meeting; 2022, **4** Tyson, SUO Meeting; 2024, **5** Li, *Nat Med*; 2024, **6** Tyson, AUA Meeting, 2024; **7** Tyson, SUO Meeting, 2023; **8** U.S. FDA. Expanded Access

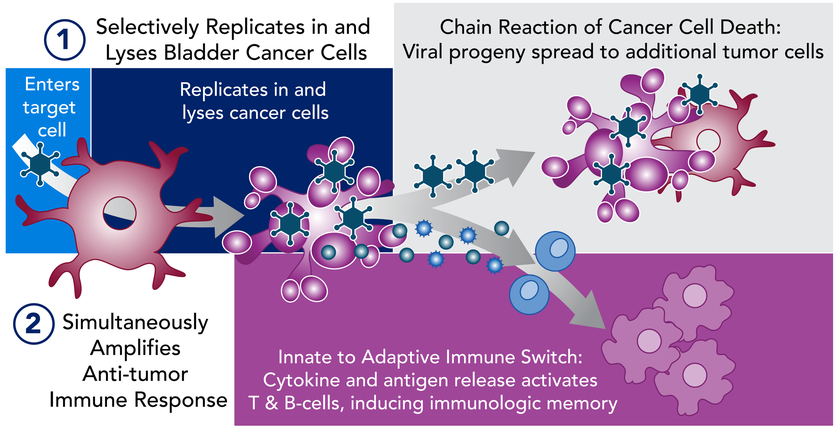
CRETO-EAP
EXPANDED ACCESS PROGRAM

Actively Enrolling

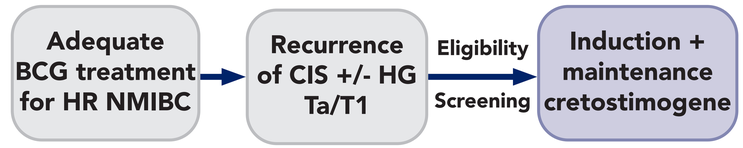
Real-World Population

Diverse Patients and Sites

Oncolytic Immunotherapy: Cretostimogene Grenadenorepvec's Dual Mechanism of Action



STUDY DESIGN



- Pragmatic entry criteria: ECOG 0-3, window for prior intravesical therapy allowed, adaptable screening process
- Eligibility and efficacy based on local assessments
- Co-primary endpoints: Safety & CR at any time
- Secondary endpoints: DoR, PFS, CFS, PROs and HRQoL

Study Administration Schedule

	Induction	Optional Re-Induction	Maintenance/Follow-Up						
Month	0	3	6	9	12	15	18	21	24
Instillation	1 2 3 4 5 6	1 2 3 (4 5 6) x6 for Non-Responder	1 2 3	1 2 3	1 2 3		1 2 3		1 2 3

- Partial responders with persistent but improved disease at week 25 or subsequent timepoints may receive continued treatment at the discretion of the Investigator
- Patients will be assessed for response during routine NMIBC surveillance, every 12 weeks during the Treatment Phase, according to AUA guidelines.

Acknowledgements: Andy Darilek, MD, Jee-Hyun Kim, PhD, John McAdory, Kara Sabourin, Kristen Scholz, DHSc, Kyle Rice, Michael Lambert, Pat Keegan, MD, MPH, Pradnya Gunjotikar, Rebecca Tregunna, MD, MBA, Shelja Patel, PharmD, Shelly Basye, MD, and Vijay Kasturi, MD

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ASCO® Genitourinary Cancers Symposium

Expanded Access Program of Cretostimogene Grenadenorepvec in Patients with Non-Muscle Invasive Bladder Cancer Unresponsive to Bacillus Calmette-Guerin

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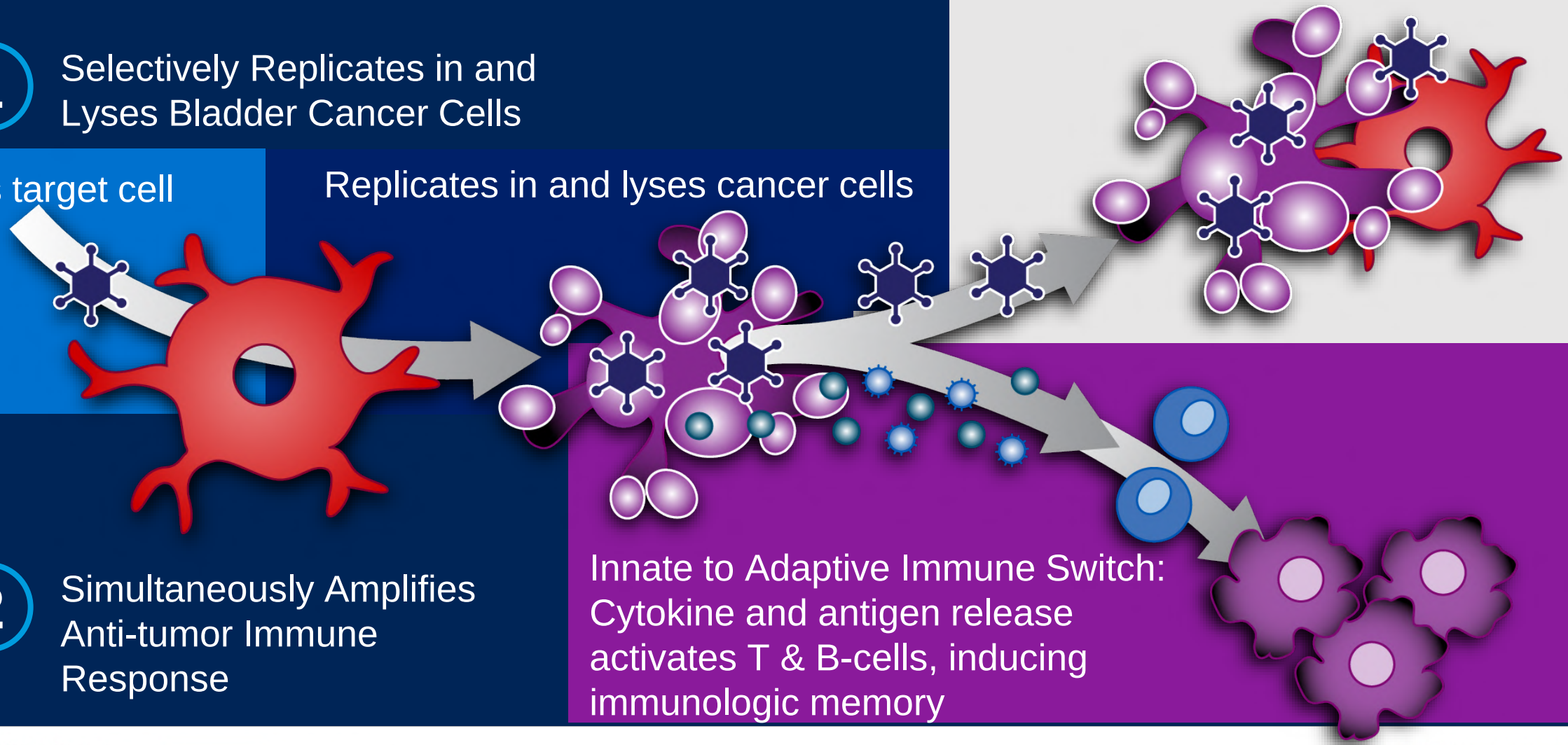
Oncolytic Immunotherapy: Cretostimogene Grenadenorepvec's Dual Mechanism of Action

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

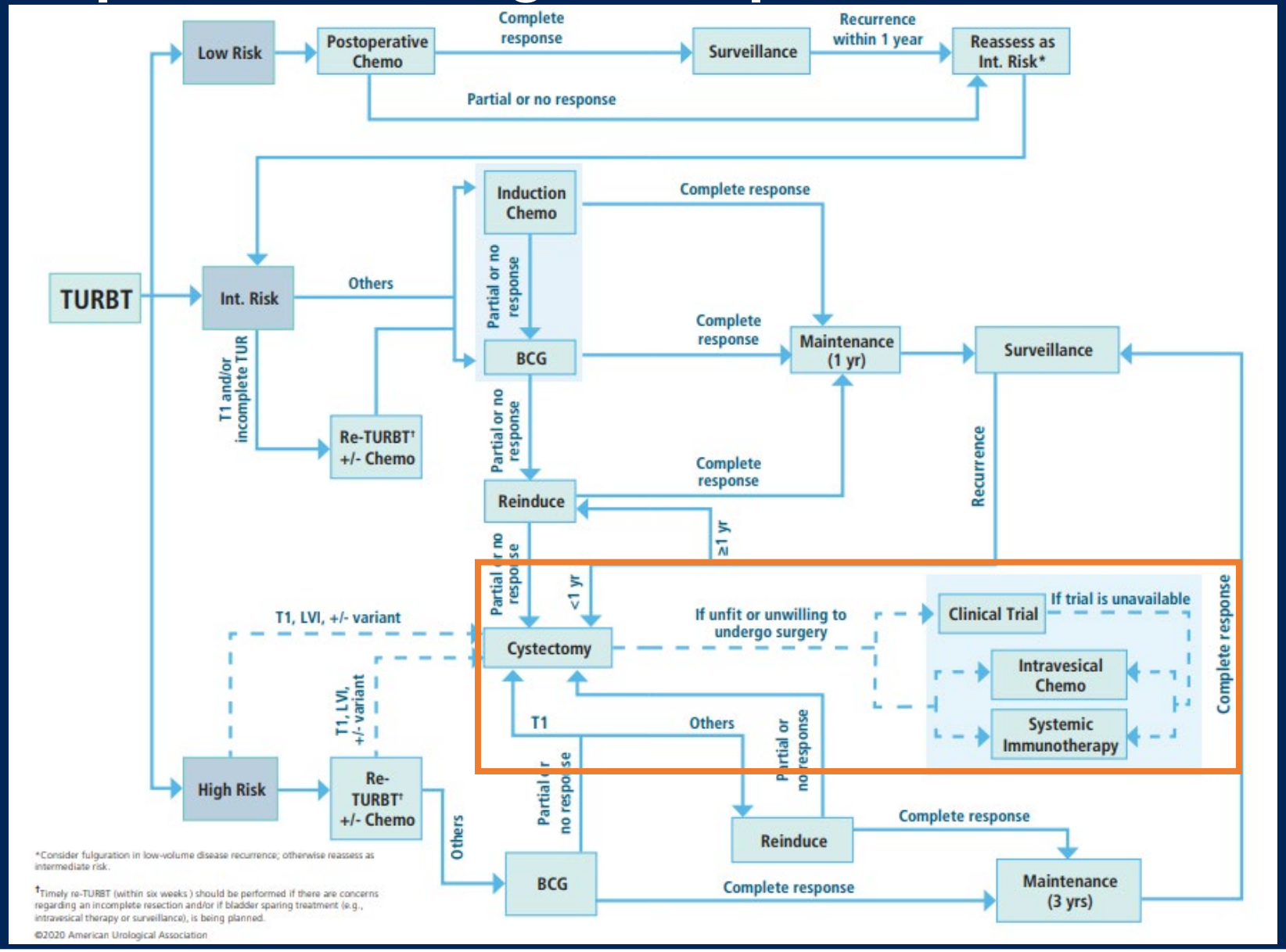


2 Simultaneously Amplifies Anti-tumor Immune Response

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

PRESENTED BY: Sarah P. Psutka, MD, MSc

BCG-Unresponsive Management per AUA/SUO Guidelines



Cretostimogene Grenadenorepvec Expanded Access Program in BCG-Unresponsive NMIBC with CIS

CRETO-EAP
EXPANDED ACCESS PROGRAM

HR BCG-Unresponsive NMIBC

Real-World, Pragmatic, Diverse Population*

- Enrollment Open
- Pathologically confirmed BCG-unresponsive CIS +/- Ta/T1 NMIBC
- All Ta/T1 and CIS disease resected as feasible prior to treatment

Cretostimogene grenadenorepvec

Single-Arm, Open-Label, IVE Administration

Study Design / 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

Co-Primary Endpoints:

Safety & CR Anytime

Additional Endpoints

- DoR
- PFS
- CFS
- PROs
- HRQoL

* Diverse population of real-world patients with high-risk, BCG-unresponsive NMIBC who may not be eligible for other clinical trials
** Patients with persistent but improved HG Ta and/or CIS at Week 25 or subsequent assessments may receive a repeat induction of 3 weekly treatments

Treatment & Assessment Schedule

- Re-induction is permitted at Month 3 for non-responders*
- Maintenance is every 3 months for year 1, every 6 months for year 2
- Patients with partial response** may receive continued doses of cretostimogene at the discretion of the Investigator

* Non-responders with CIS, HG Ta, or CIS+HG Ta . Patients with T1 recurrence must discontinue.
** Partial Response - Patients with persistent but improved CIS, HG Ta or CIS + HG Ta without T1 or higher stage urothelial carcinoma at Week 25 or subsequent timepoints

Key Takeaways

- Oncolytic immunotherapy with dual MOA
  - Postulated innate to adaptive immune switching
- Cretostimogene is a potentially effective, well tolerated, and durable regimen
- Easily fits within existing clinic workflow
- CRETO-EAP is actively enrolling patients with HR BCG-UR CIS +/- Ta/T1 from geographical diverse sites
- Real world, socioeconomically diverse population who may not qualify for other HR BCG-UR clinical trials