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

Gary D. Steinberg, MD

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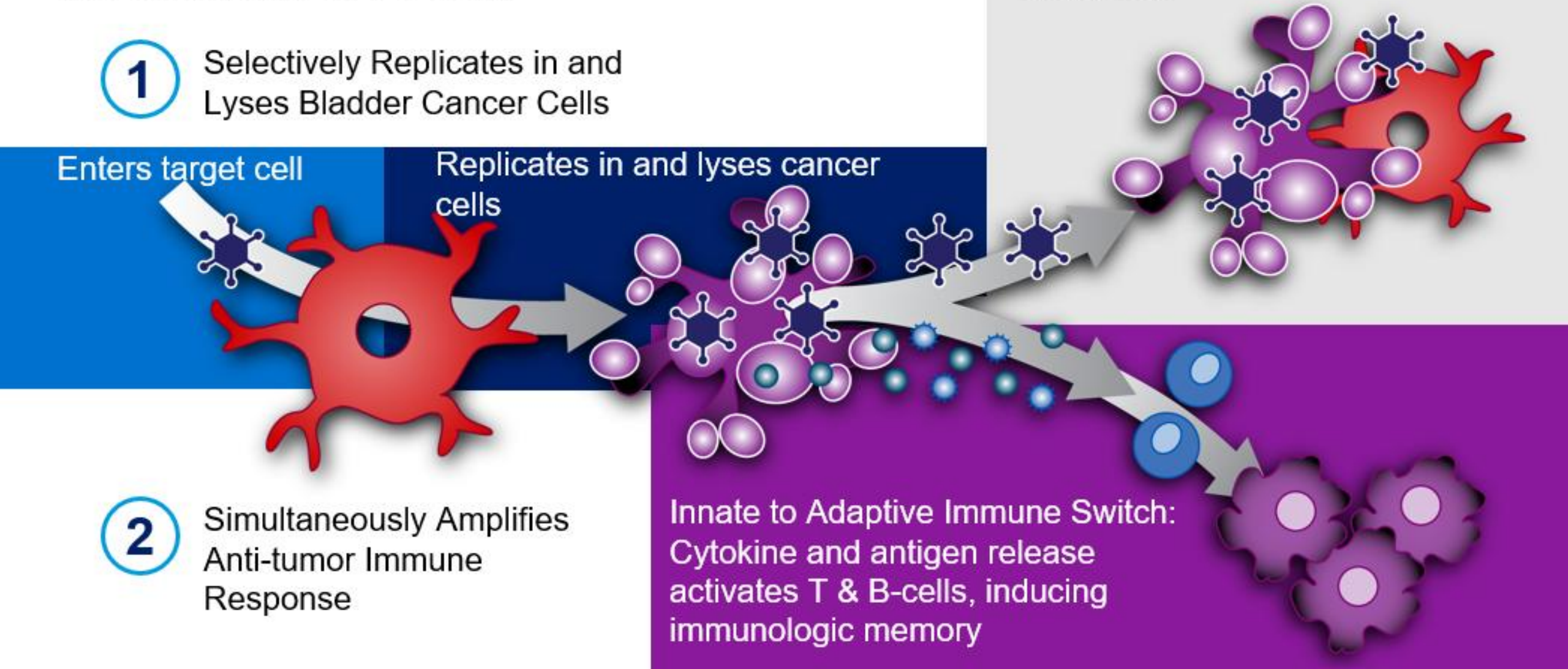
Disclosures

- CG Oncology – No conflict of interest

Oncolytic Immunotherapy: Cretostimogene Grenadenorepvec's Dual Mechanism of Action

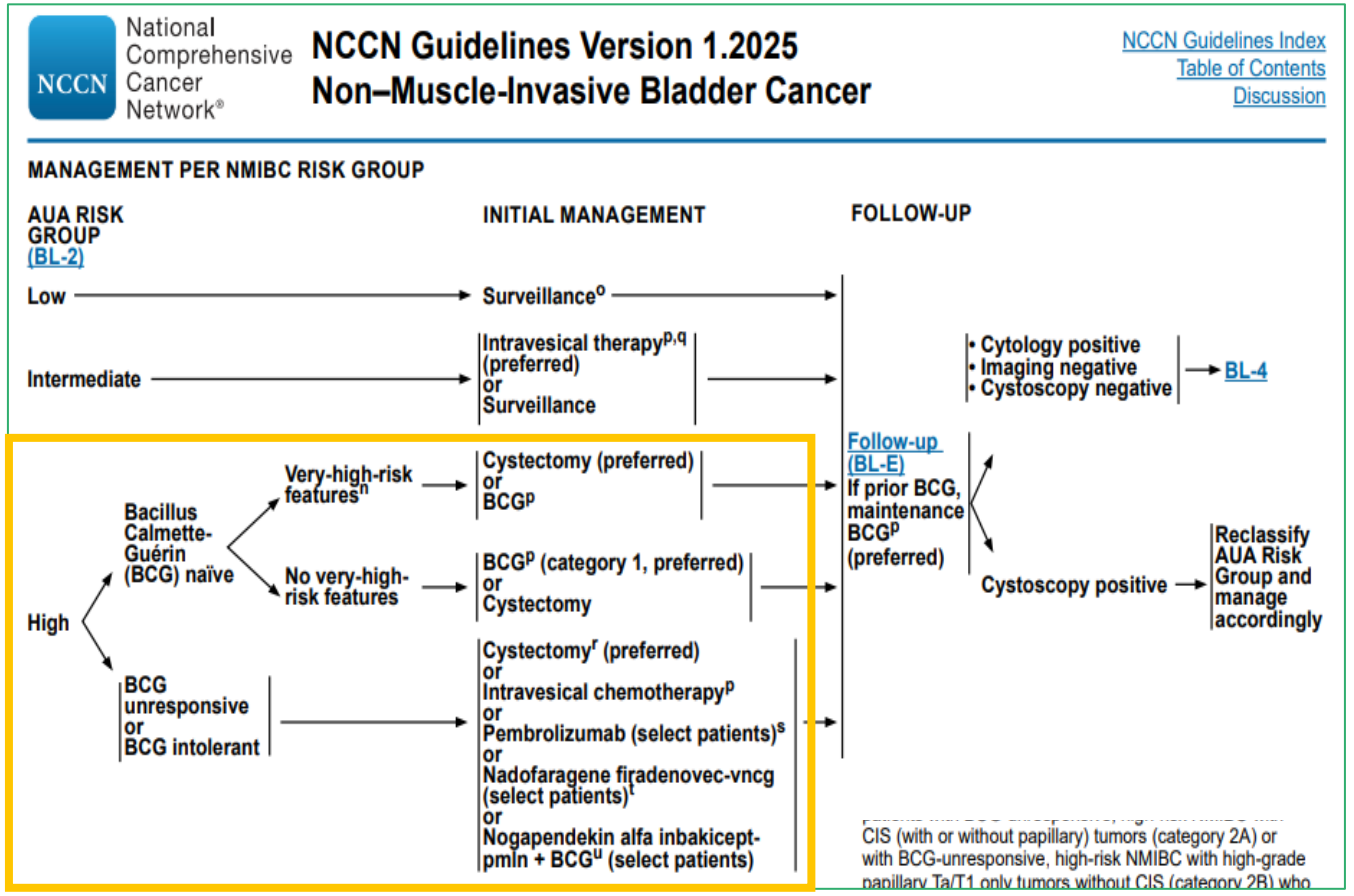
1. Selectively Replicates in and Lyses Bladder Cancer Cells



2. Simultaneously Amplifies Anti-tumor Immune Response

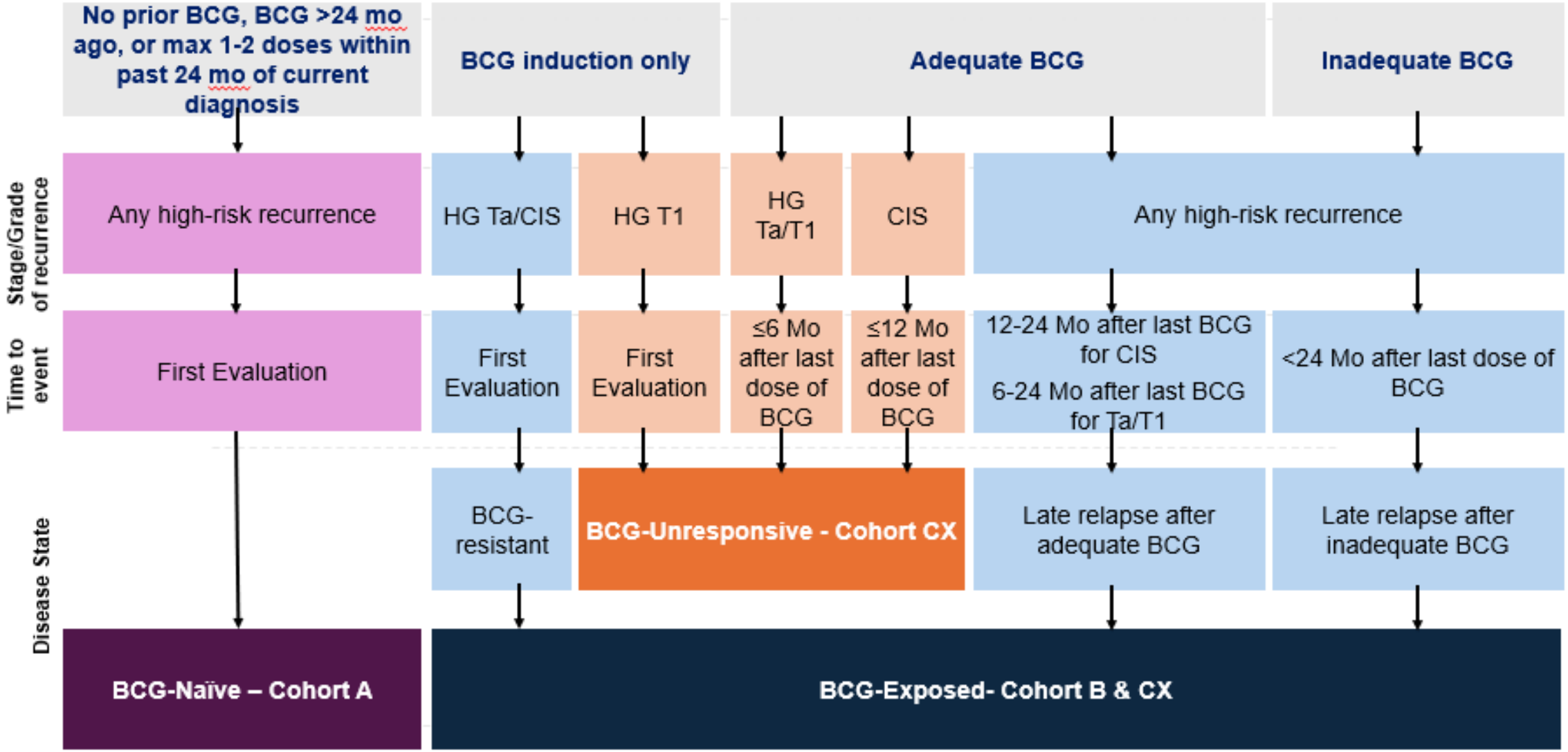
Considerable Unmet Needs in High-Risk NMIBC

- Guidelines currently recommend IVE BCG or radical cystectomy
- **Challenges with BCG**
  - Despite high initial response rates, over 50% of patients will recur[1]
  - 20-40% are at risk for progression[2,3]
  - Ongoing BCG shortages[4]
- **Risks with radical cystectomy**
  - Post-operative complications[5,6]
  - Impact on quality of life[6]



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. Holzbeierlein J, Bixler BR, Buckley DI, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline: 2024 amendment. J Urol. 2024;10.1097/JU.0000000000003846. 5. Maibom SL, et al. BMJ Open.2021 Apr 14;11(4):e043266. doi: 10.1136/bmjopen-2020-043266. 6 Clements M, et al. Eur Urol. 2021;81(3), 294-304. https://doi.org/10.1016/j.eururo.2021.09.018

Broad High-Risk* NMIBC Study Population



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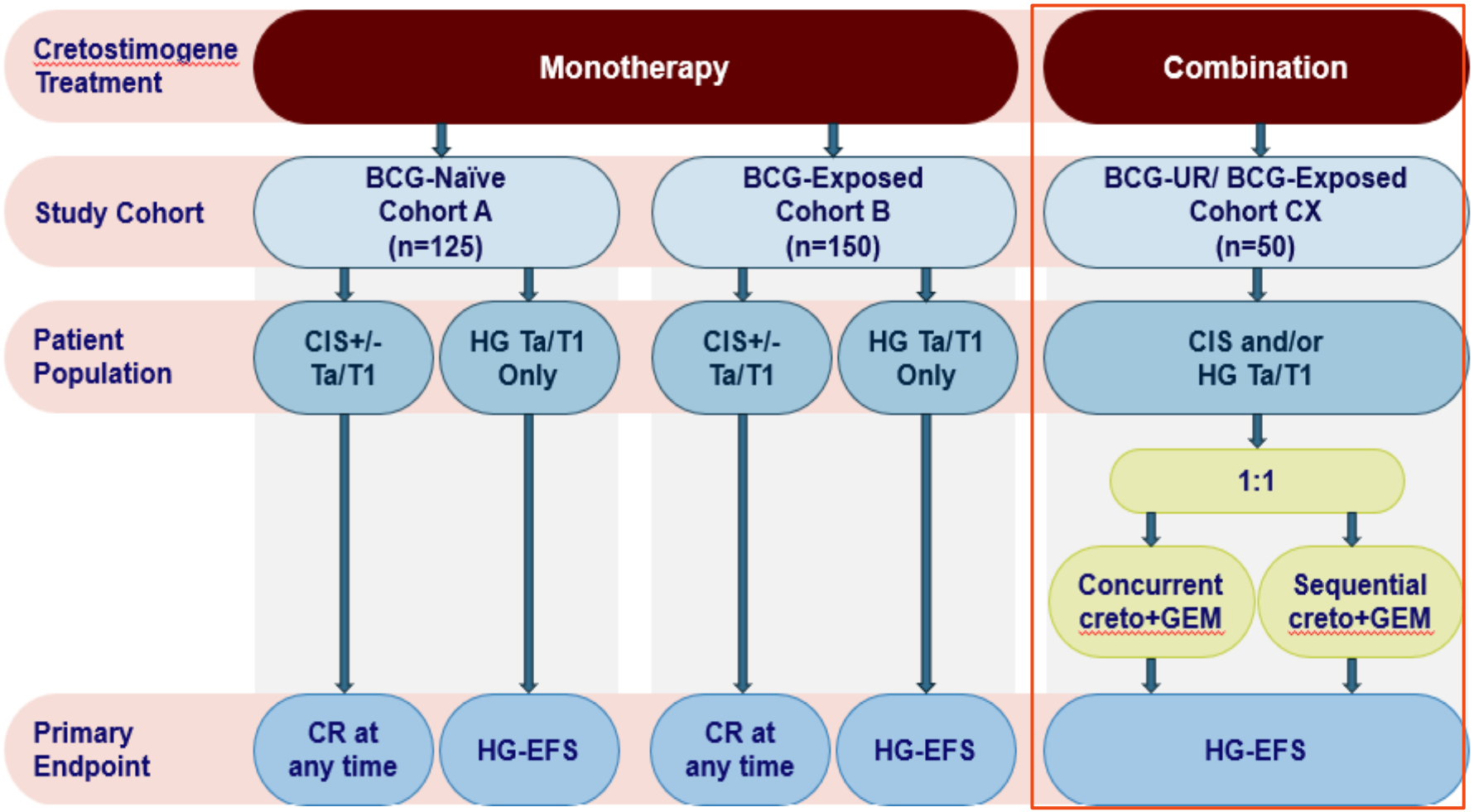
* High-Risk NMIBC eligibility per AUA/SUO guideline criteria

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.

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



Key Secondary Endpoints
Duration of Response
All-Cause Event Free Survival
Bladder Cancer Specific Survival
Cystectomy-Free Survival
Safety
Tolerability

CORE-008 will investigate cretostimogene as monotherapy, and in rational combinations, in a broad HR NMIBC population (BCG-Naïve, Exposed & Unresponsive)

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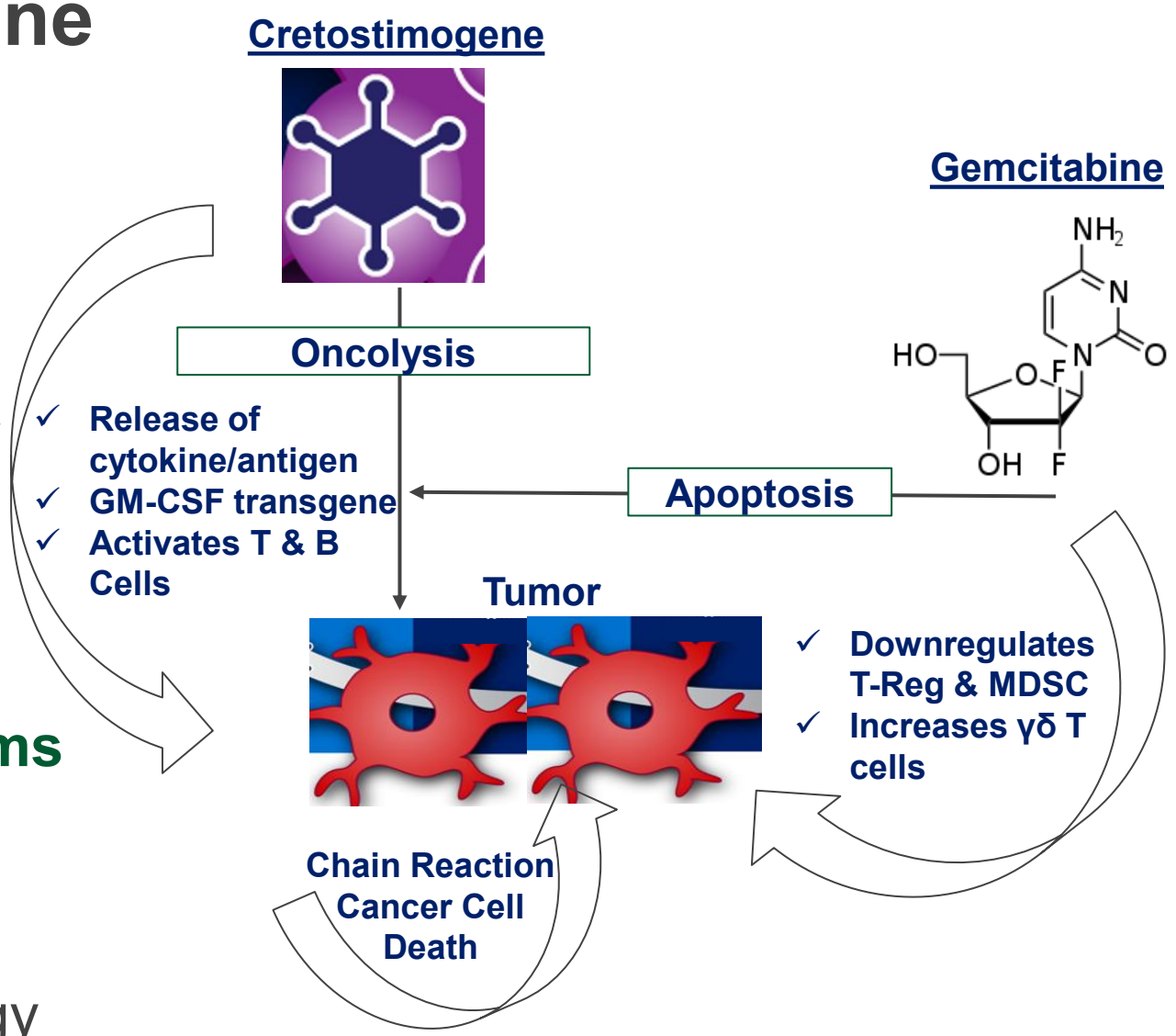
* BCG-naïve includes no prior treatment with BCG, no BCG within past 24 mo prior to current diagnosis, or maximum 1-2 doses of BCG within past 24 mo prior to current diagnosis
** BCG exposed includes BCG resistant and delayed relapse after adequate and inadequate BCG
BCG-Bacillus Calmette-Guerin, CIS- Carcinoma in Situ, CR- Complete Response, HG-EFS- High-Grade Event-free survival, GEM- intravesical gemcitabine
NCT06567743

Cohort CX: Possible Synergism Between Cretostimogene & Gemcitabine

- Efficacy, safety, and tolerability demonstrated as monotherapy and in combination
- Pre-clinical synergy with gem and oncolytic immunotherapy in other tumor types
- Prior phase 1-3 studies of gem+ immunotherapy in high-risk NMIBC
- **Proposed complementary mechanisms of action**
  - Direct oncolytic and pro-apoptotic effects
  - Potential immune modulating synergy



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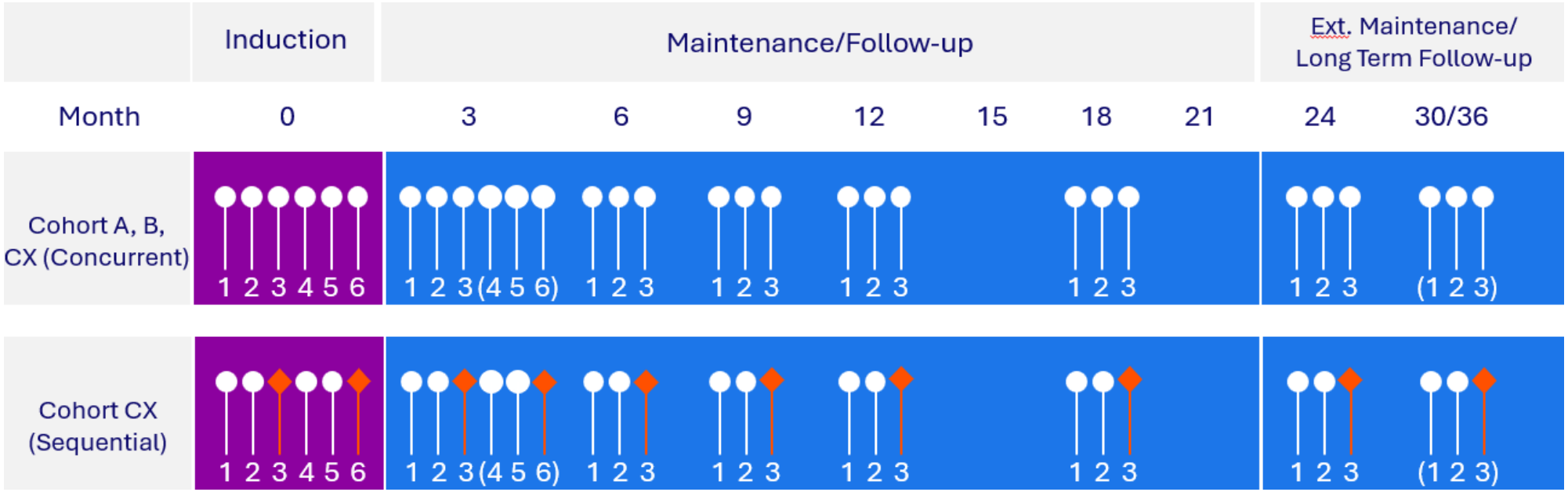
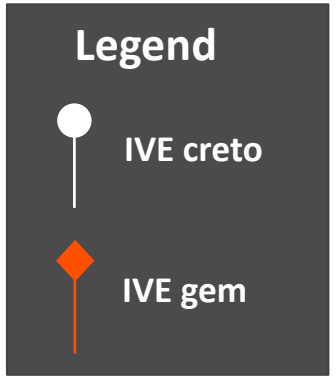
MDSC= Myeloid-dervied supressor cells

1.Skinner E, et al. *J Urol.* 2013; 10(4):1200-04. 2. Alam S, et al. *Clin Cancer Res*. 2024(30):10-suppl. 3.Gujar SA, et al. *OncoImmunology.* 2013;2:e27622.

Treatment & Assessment Schedule





- Cystoscopy & Cytology every 3 months
- 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

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Key Eligibility Criteria

Inclusion Criteria
• HR NMIBC, AUA definition
• BCG-naïve (**Cohort A**)
• BCG-exposed (**Cohort B**)
• BCG-exposed & BCG-unresponsive (**Cohort CX**)
• Complete TURBT within 90 days
• Adult, ECOG 0-2
• Willing to use contraception, comply with procedures
• Adequate organ function

Exclusion Criteria
• MIBC, Nodal or Metastatic UC
• UC in upper tract or urethra within 24 months
• Any history of T3 or higher in upper tract/T2 within 4 years
• Prior systemic treatment, radiation, or surgery (beyond TURBT) for bladder cancer
• Intravesical therapy within 90 days • For Cohort CX- systemic or IVE gemcitabine within 2 yrs except single perioperative instillations
• Antiplatelet/anticoagulation, antiviral or immunosuppressive meds that can't be held
• Transplant, AIDS, active Hep B/C, malignancy, active infection
• Live vaccine, within 30 days
• Not recovered from AE's, condition that contraindicates study, pregnant/breastfeeding (or planning to), can't tolerate study procedures

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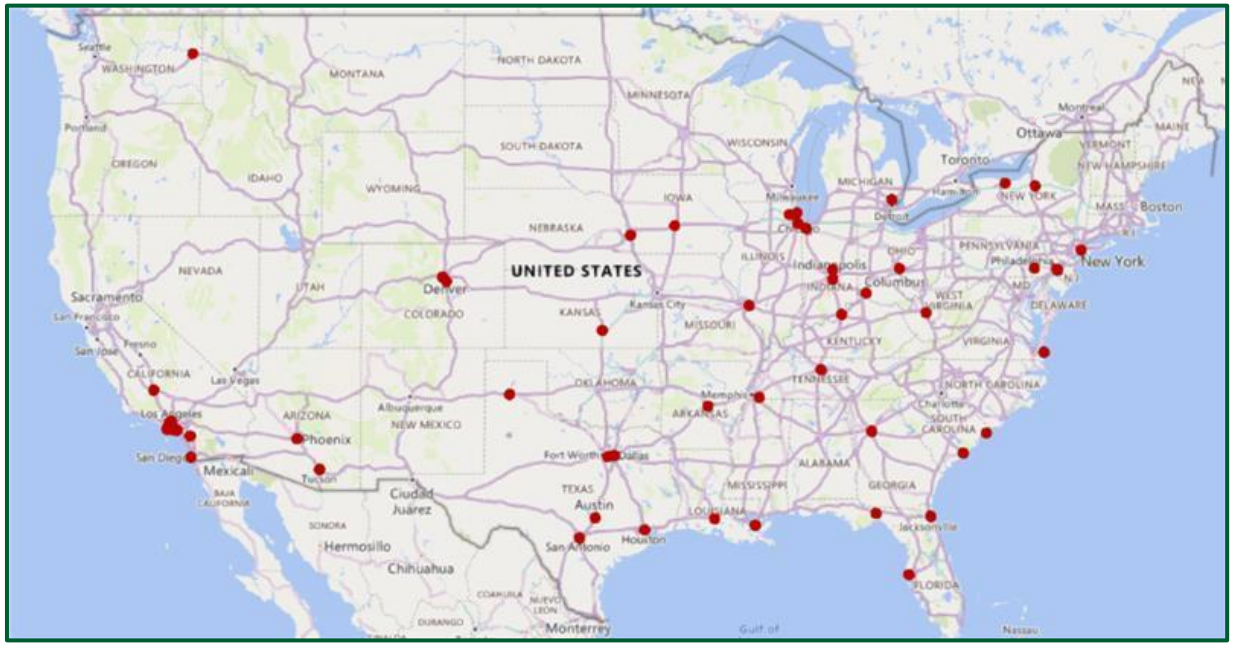
CORE-008 is Currently Ongoing & Actively Enrolling

- As of October 2025:
  - **Cohort A (BCG-Naïve)**
    - **CIS containing arms have completed enrollment**
    - **HG Ta/T1 arm planned**
  - Cohort B (BCG-Exposed) is planned and received collaborative SUO-CTC support
  - **Cohort CX (BCG-Exposed & BCG-UR)- completed enrollment**
- **First results Cohort A 2H2025**



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Thank You

All Bladder Cancer Patients and Their Families

Key Investigators, Study Coordinators, Nurses

Key Collaborators

Trinity Bivalacqua, UP, PA

Siamak Daneshmand, USC, CA

Neal Shore, CURC, SC

Shreyas Joshi, Emory, GA

Colin Dinney, MDACC, TX

CG Oncology

Andy Darilek

Jee-Hyun Kim

Pradnya Gunjotikar

Kristen Scholz

Rebecca Tregunna

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