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Trial in Progress: PIVOT-006- A Phase 3, Randomized Study of Adjuvant Intravesical Cretostimogene Grenadenorepvec Versus Surveillance for the Treatment of Intermediate-Risk NMIBC

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Disclosures

- Consulting/Advisory Boards: Urogen, Aura, Merck, ImmunityBio, CAPSMedical, Janssen, Merck, Pfizer, BMS, Protara
- Honorarium: UroToday, UrologyTimes, AUA, Kaplan, BCAN
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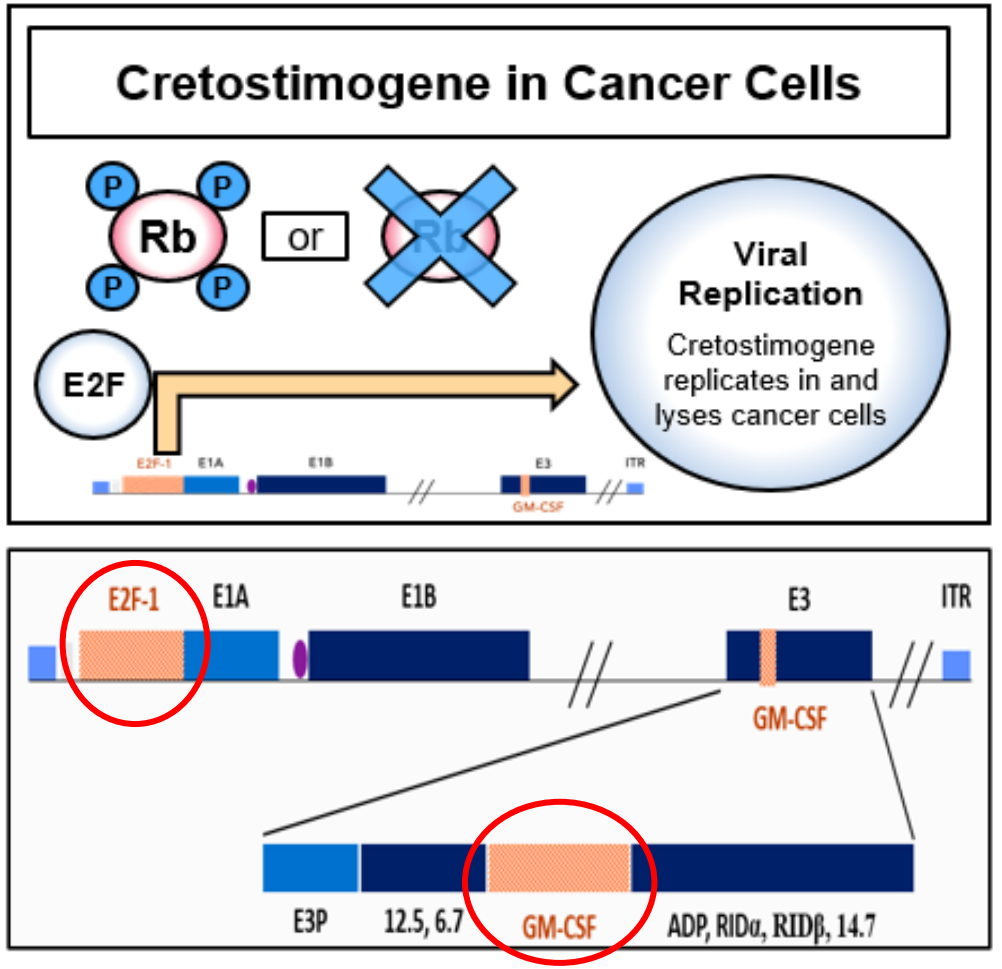
- Study Chair for EA8212

Cretostimogene Selectively Targets Rb-E2F Pathway Altered Cancers

- **Oncolytic immunotherapy with dual MOA**
  - Viral replication results in tumor lysis
  - Stimulation of immune response
- Conditionally replicating, highly immunogenic adenovirus
  - Under regulation of the **human E2F-1 promoter**
  - Encodes **GM-CSF transgene**



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

Significant Unmet Need with High Prevalence of Intermediate-Risk NMIBC in the U.S.

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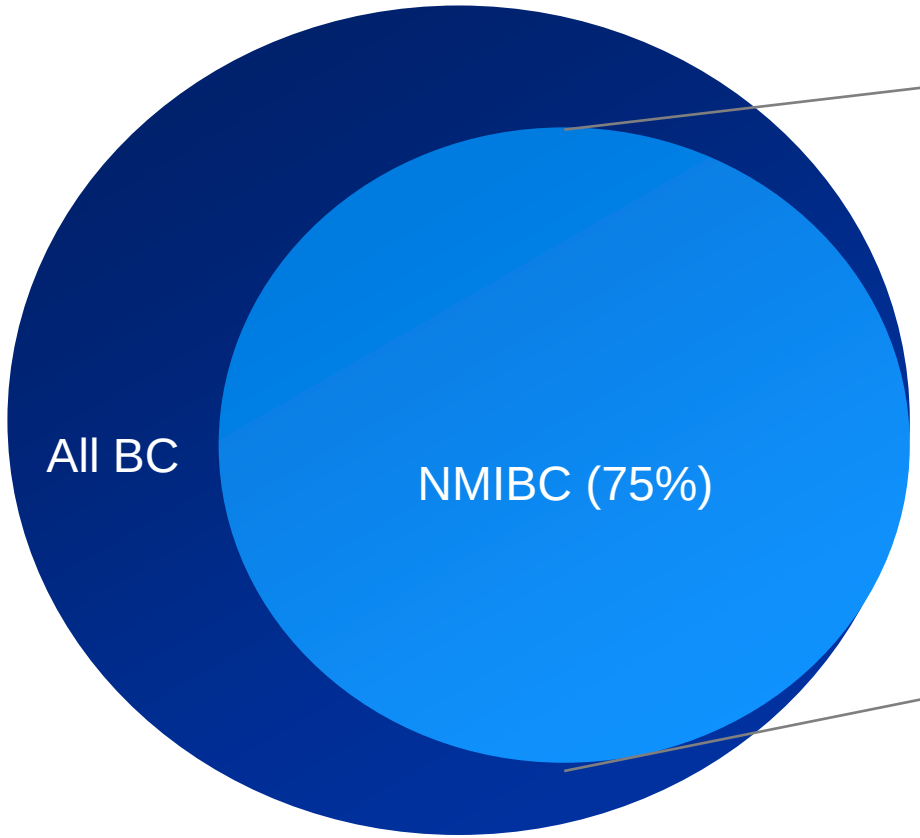
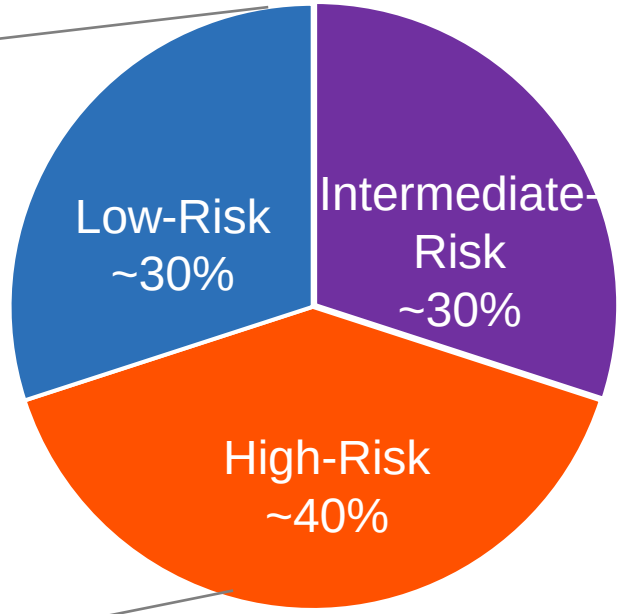
NMIBC Prevalence in U.S. [1]



NMIBC Risk Stratification

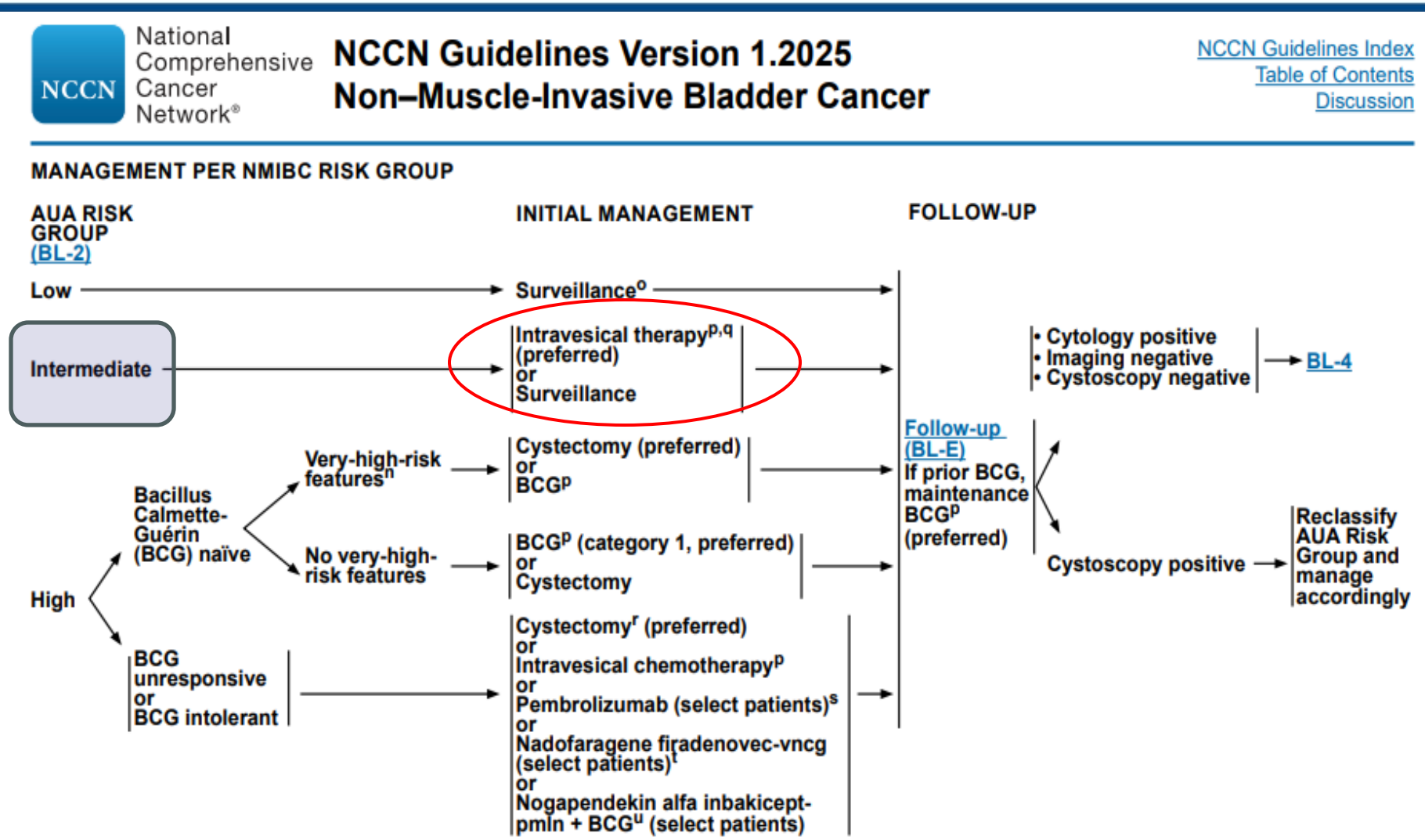


Intermediate-Risk NMIBC:

- **High Recurrence**; 50-70%[2]
- Low Progression; < 5%[2]
- Common[2]
- Costly[3]
- Chronic[4]
- Risk of Anesthesia, Surgery[5]

BC- Bladder Cancer; NMIBC- Non-Muscle Invasive Bladder Cancer
[1] SEER Cancer Stat Facts: Bladder Cancer [2] Babjuk, et al. *Eur Uro;* 2019 [3] Mossanen, et al. *World J Urol;* 2019 [4] Sharma, et al. *J Uro;* 2021, Suppl 3
[5] Erikson, et al. *Scand J Uro;* 2020

Management of Intermediate-Risk NMIBC

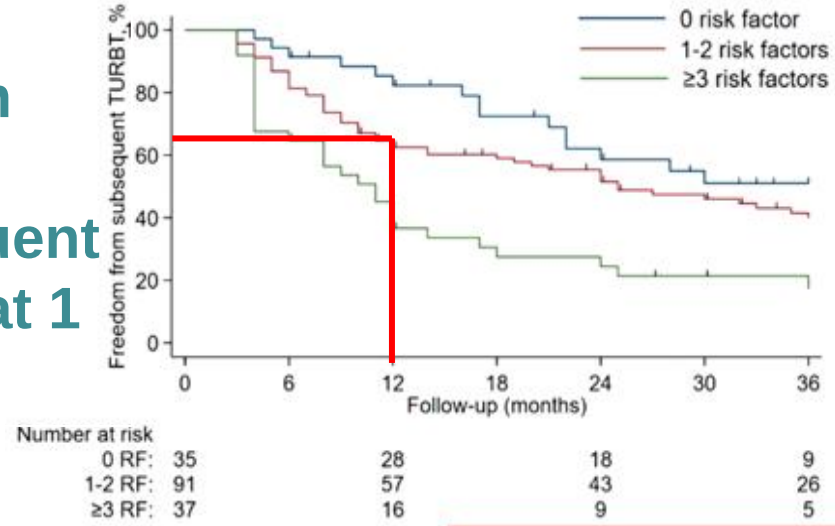


Experience with TURBT with Surveillance in NMIBC

EAU24 | PARIS, FRANCE 5-8 April 2024

Results

63% Freedom from Subsequent TURBT at 1 Year



Median Time on AS	
o RF	28 months (IQR 12-36)
≥ 3 RF	15 months (IQR 4-18)

Table 2. *Estimated Kaplan-Meier Survivor Function for Freedom of Subsequent Transurethral Resection of Bladder Tumor Stratified According to International Bladder Cancer Group Intermediate-risk Non-muscle Invasive Bladder Cancer Scoring System*

Variable	Overall (n=163)	0 RF (n=35)	1-2 RF (n=91)	≥3 RF (n=37)
6 months, % (95% CI)	80 (73-85)	91 (76-97)	81 (72-88)	65 (47-78)
12 months, % (95% CI)	61 (53-68)	82 (65-92)	63 (52-72)	37 (21-52)
24 months, % (95% CI)	47 (39-55)	59 (39-74)	51 (41-61)	24 (12-40)
36 months, % (95% CI)	37 (29-45)	51 (32-67)	40 (29-50)	17 (6-32)

R. Contieri

The International Bladder Cancer Group Intermediate-risk Non-muscle Invasive Bladder Cancer (IBCG IR-NMIBC) scoring system predicts the need for intervention fo patients on active surveillance.

www.eau24.org

European Association of Urology

Contieri R., et al. Eur Urol Suppl 2024;85 (S1): S1717

Intermediate-Risk NMIBC Study Considerations

- **IR-NMIBC is a challenging disease state**
  - Disease is heterogenous
  - Guidelines recommendations are mixed; Limited adjuvant options
- **PIVOT-006 is one of the first adjuvant, RCTs in IR-NMIBC**
- **Surveillance as a comparator offers advantages**
  - Reflects true effect size of adjuvant therapy
  - Underscores natural history of disease state
  - Enables efficient and streamlined clinical trial execution

Phase 3 Adjuvant Cretostimogene vs Surveillance for Intermediate-Risk NMIBC

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N = Up to 364

Design: Open-label, RCT

Regimen*: IVE cretostimogene Induction (Weekly x 6) & 1- yr Maintenance following TURBT

Endpoints: RFS (primary), RFS at 12-month and 24-month, PFS, & Safety

Trial Type: Phase 3

Exploratory: Biomarkers, PROs, HRQoL

Key Entry Criteria

- IR-NMIBC
  - Solitary LG Ta >3cm
  - Multifocal LG Ta
  - LG T1
  - LG Recurrent < 1 yr
  - HG Ta ≤ 3cm
- Complete resection at baseline
- Adequate organ function
- ECOG 0-2

1:1 Randomization

Stratification:
Perioperative Chemo,
HG vs LG

Geography:
North America

Arm A: cretostimogene after TURBT

Disease Assessment:
Every 3 mos cystoscopy & cytology, for 2 years; then every 6 mos starting Year 3

Arm B: complete TURBT alone

Arm B patients offered cretostimogene treatment following IR-NMIBC recurrence

IVE= Intravesical; HRQoL= Health-Related Quality of Life; PRO= Patient-Reported Outcomes; RCT= Randomized Controlled Trial; RFS= Recurrence-Free Survival
* Induction= Weekly x 6; Maintenance= Weekly x 3 at Mos 3, 6 and x 1 at Mos 9, 12

Exclusion Criteria

- Current or prior evidence of **HR-NMIBC** defined as:
  - HG T1
  - HG Ta > 3 cm that is recurrent or multifocal
  - Any *carcinoma in situ* (CIS)
  - Any variant histology
  - Any HG prostatic urethral involvement
  - Any LVI
  - Any BCG treatment failure in HG patient
- LR-NMIBC
  - A LG solitary, Ta ≤ 3 cm lesion that has recurred more than 12 mos after a previous IR-NMIBC diagnosis
- Has **IR-NMIBC** that **cannot be completely resected**
- Has hx of **MIBC**, Nodal or Metastatic disease

Efficacy Assessments

- **Efficacy Assessments**
  - Visit, cystoscopy, biopsy for cause, cytology
    - Q3mo, first 2 years
    - Q6mo, 3rd year
  - Imaging
    - Q12mo
  - Mapping biopsy/imaging for isolated positive cytology
  - Local & central pathology review

- **Recurrence Free Assessment**
  - Without recurrence or progression in the bladder
  - Upper tract or prostatic urethra

Strong Enrollment Momentum on PIVOT-006

- SUO-CTC trial
- Diverse representation across LUGPA & Academic sites
- First enrollments January 2024
- **Ahead of expected enrollment period**
- Anticipate completing enrollment late 2025-early 2026

Acknowledgements

All Bladder Cancer Patients and Their Families

The Study Coordinators and Nurses

Key Collaborators

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Thank You

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