

CRETOSTIMOGENE GRENADENOREPVEC

Mechanism, Emerging Clinical
Evidence, and Considerations for
Practice Integration in Non-Muscle
Invasive Bladder Cancer



Attacking Bladder Cancer
for a Better Tomorrow™

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Specialty Networks Bladder & Kidney Cancer Workshop



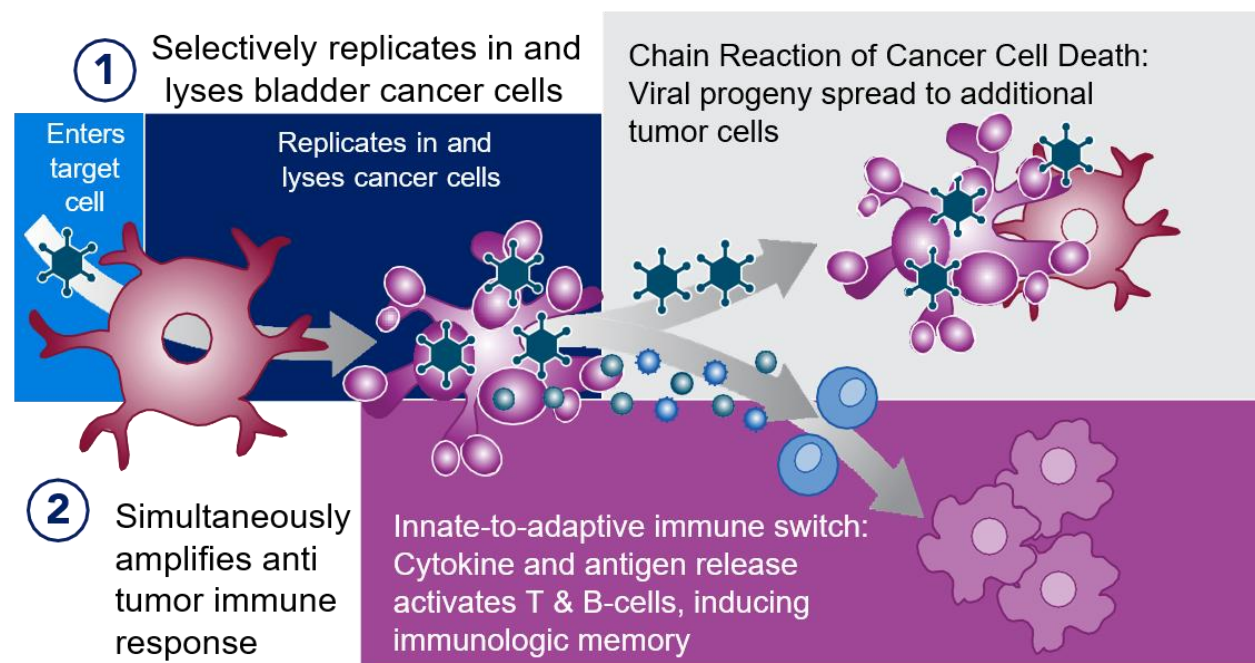
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Cretostimogene Grenadenorepvec's Dual Mechanism of Action

- Cretostimogene selectively replicates in and lyses bladder cancer cells while amplifying the immune response against bladder tumors
- Novel, effective, well-tolerated intravesical therapy being investigated across intermediate and high-risk NMIBC



	Induction	Optional Reinduction	Maintenance/Follow-Up						Ext. Maintenance/ Long-Term Follow-up
Month	0	3	6	9	12	15	18	21	24/30/36
Instillation	● 1 ● 2 ● 3 ● 4 ● 5 ● 6	● 1 ● 2 ● 3 ● 4 ● 5 ● 6	● 1 ● 2 ● 3	● 1 ● 2 ● 3	● 1 ● 2 ● 3		● 1 ● 2 ● 3		● 1 ● 2 ● 3

Cretostimogene Programs Across High-Risk & Intermediate Risk NMIBC Addresses Significant Unmet Need

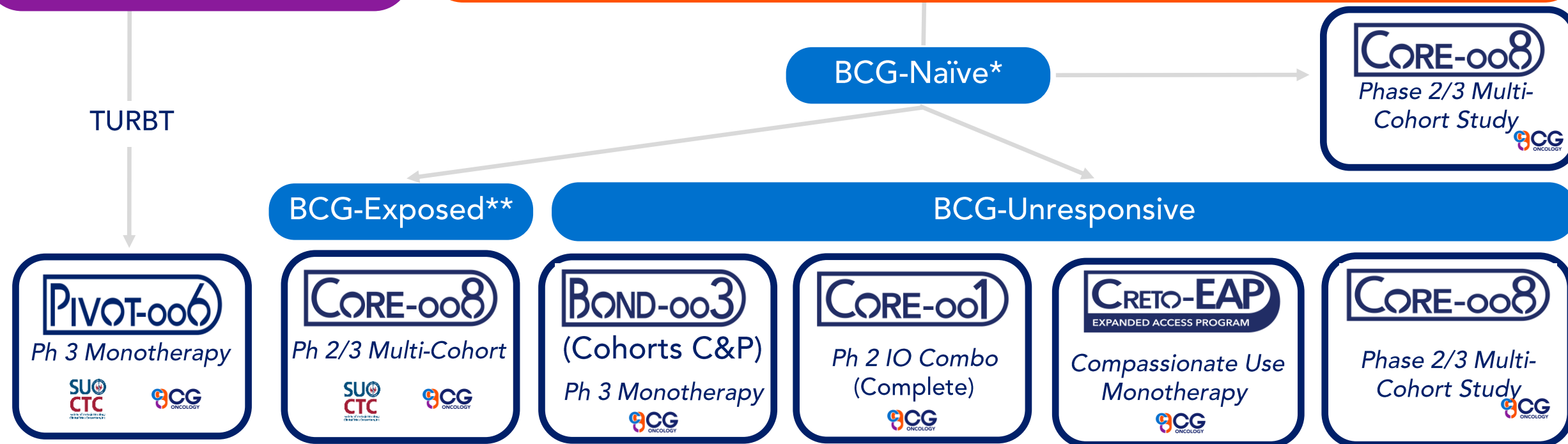
NMIBC

Intermediate-Risk

- LG Ta- multifocal OR solitary >3 cm OR recurrence < 12 mo
- HG Ta- solitary AND primary AND ≤ 3 cm
- LG T1

High-Risk

- CIS
- BCG unresponsive
- HG Ta: multifocal OR recurrent OR > 3 cm
- HG T1
- Variant histology (<50% for trial inclusion)

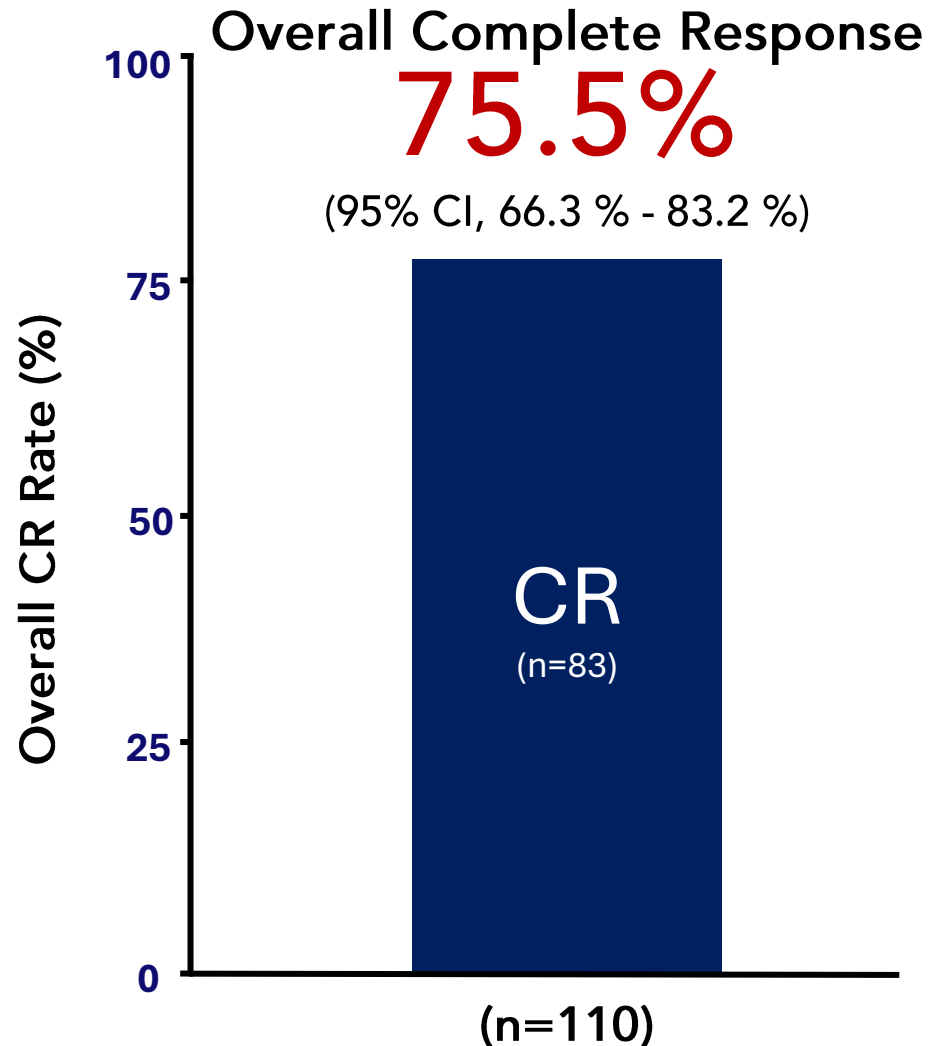


* BCG-naïve includes no prior treatment with BCG, no BCG within past 24 mo prior to current diagnosis, or maximum 1-2 doses of BCG within past 24 mo prior to current diagnosis

** BCG exposed includes BCG resistant and delayed relapse after adequate and inadequate BCG

± Diverse population of real-world patients with high-risk BCG-unresponsive NMIBC who may not be eligible for other clinical trials

Phase 3 Cretostimogene Monotherapy for High-Risk BCG-Unresponsive NMIBC with CIS



THE LANCET Oncology
Tyson, M.D., et al, 2026

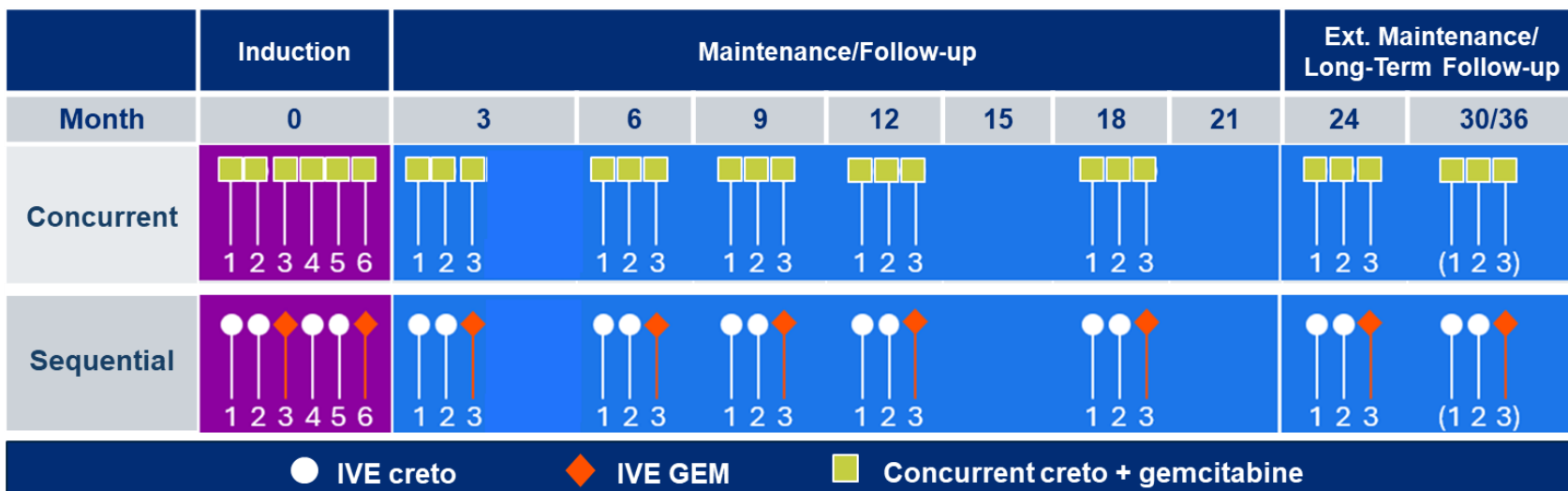


CR Landmark	CR Rate, % (95% CI)	K-M Est, % (95% CI)
12-month	46.4% (36.9, 56.1) <i>51 out of 110 patients</i>	50.7% (40.9, 59.8)
24-month ¹	41.8% (32.5, 51.6) <i>46 out of 110 patients</i>	42.4% (32.7, 51.7)

- 97.3% free from progression to MIBC at Month 24
- 84.5% avoided radical cystectomy by Month 24
 - Among RCs, 82.4% (14/17) were T0 or NMIBC
- All Complete Responses are centrally confirmed²
 - Local: Central concordance: 96.3% of assessments
- No grade 3 or higher TRAEs, deaths, discontinuations

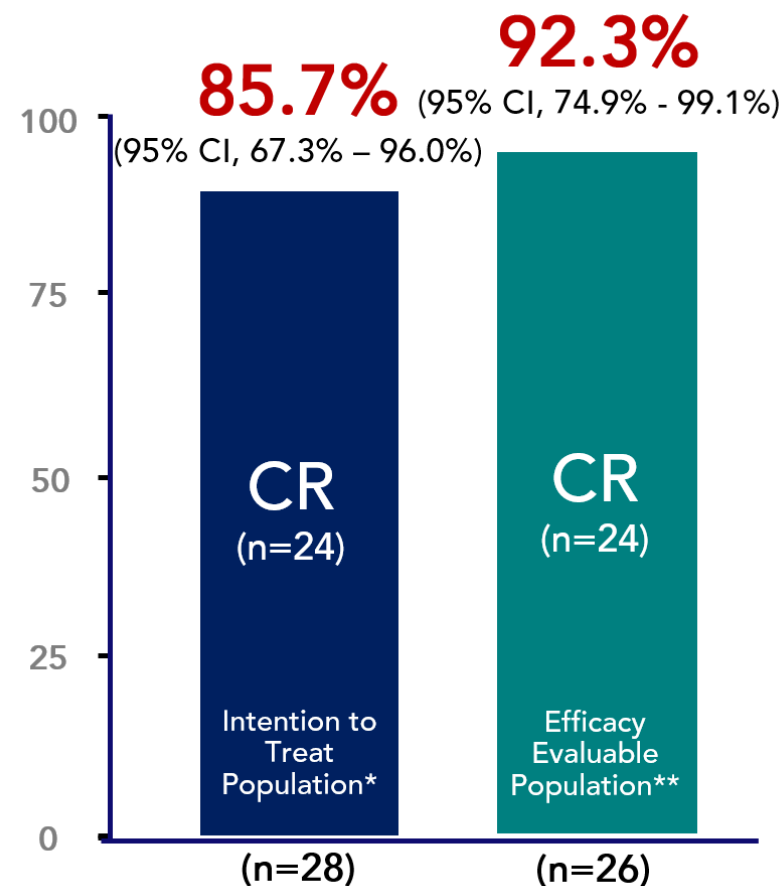
Efficacy data cutoff as of 14MAR2025. Efficacy analysis centrally confirmed. All patients have active disease at baseline prior to enrollment. Received adequate BCG per FDA 2018 guidance; ¹ 24-mo data based on 23JUN2025 data cutoff. ² A CR is defined as having a negative cystoscopy, a negative urine cytology, and a negative biopsy. In addition, all patients at 12-month timepoint undergo mandatory, systematic bladder mapping of 5 locations, biopsy of the prostatic urethra, and upper tract imaging to confirm CR and detect potential occult disease in the bladder. Analysis based on both landmark CR rate assessed in clinical trial and CR by Kaplan-Meier estimate.

Phase 2, Cretostimogene Combination Therapy for High-Risk BCG-Exposed or BCG-Unresponsive NMIBC



- Includes BCG-Exposed and BCG-Unresponsive patients
- High CR rates were achieved in both concurrent and sequential arms
- No treatment-related progression to MIBC or mUC
- No grade 3 or higher TRAEs, SAEs, or deaths

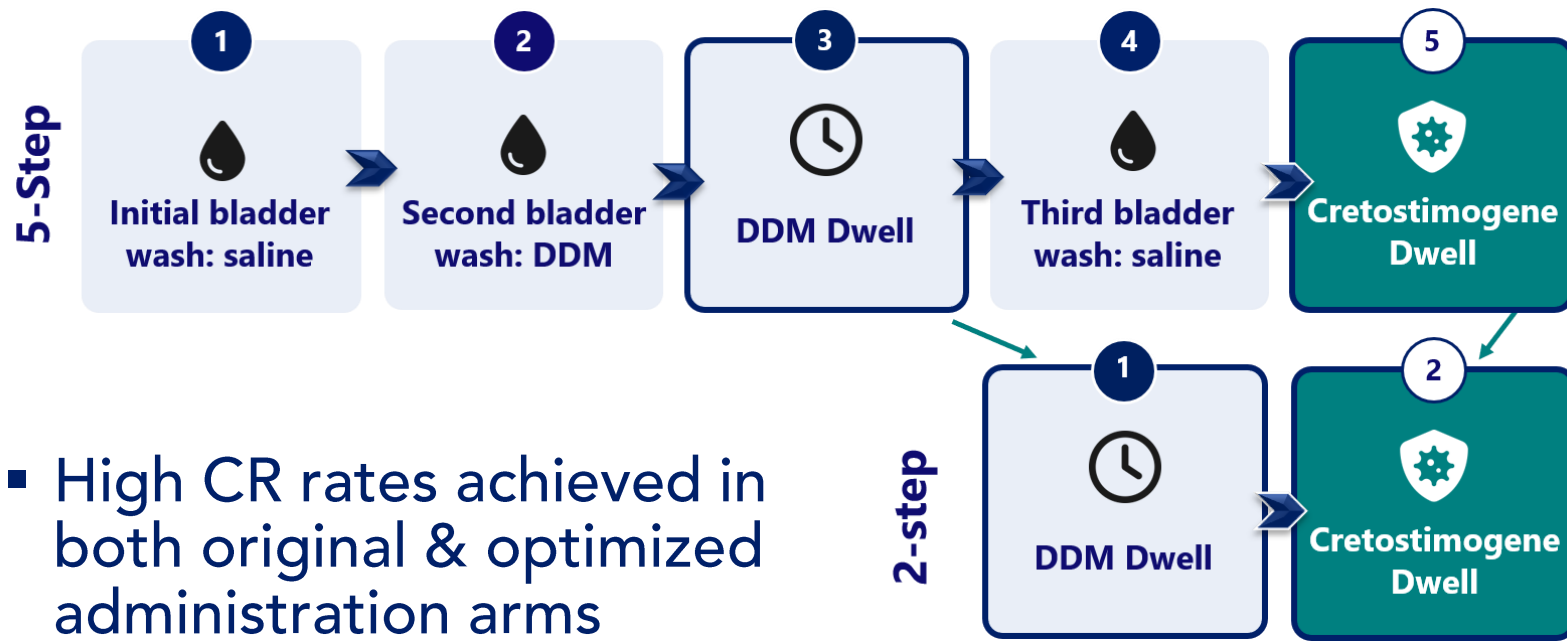
Complete Response at Any Time (%)



CIS= Carcinoma in Situ; CR=Complete Response; CR defined as having negative cystoscopy, urine cytology, and biopsy (as indicated); Efficacy data cutoff as of 13MAR2026. Efficacy assessments based on local pathology review; * Intention to treatment (ITT) population includes all participants who are randomized in Cohort CX (Arm 1/Concurrent; Arm 2/Sequential).

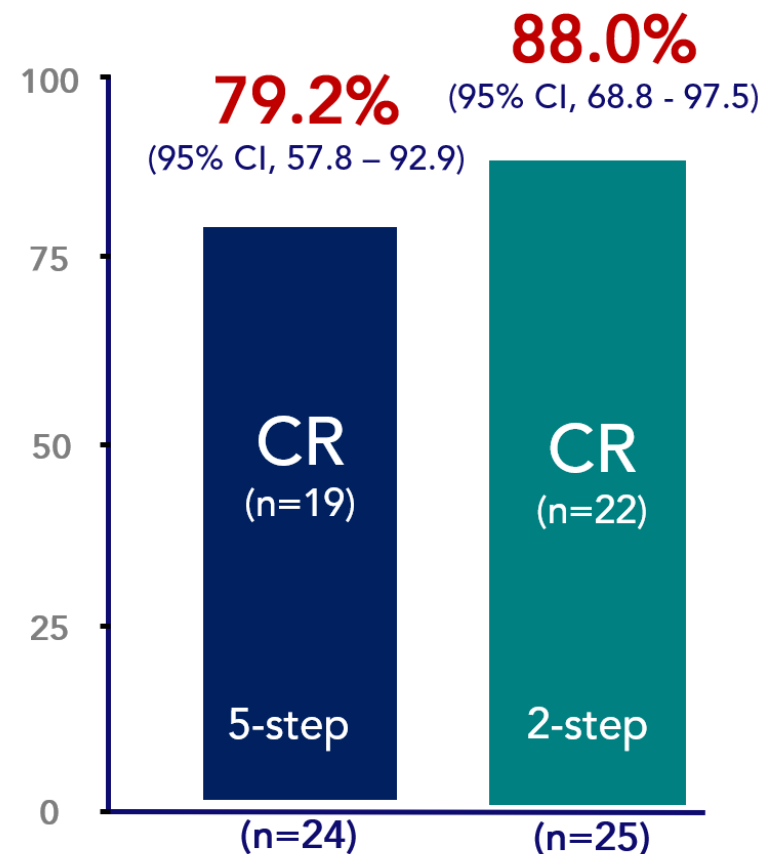
** Efficacy evaluable population includes patients who have received at least four doses of cretostimogene, meet the definition of BCG-Unresponsive/BCG-Exposed and have completed a protocol-defined efficacy assessment at Month 3

Phase 2, Cretostimogene Monotherapy for High-Risk BCG-Naive NMIBC



- High CR rates achieved in both original & optimized administration arms
- No treatment-related progression to MIBC or mUC
- No grade 3 or higher TRAEs, SAEs, or deaths
- 98% (53/54) completed all protocol defined treatments

Complete Response at Any Time (%)



Efficacy data cutoff as of 01SEP2025. Efficacy analysis centrally confirmed. All patients have active disease at baseline prior to enrollment.

* 49 patients were assessed for efficacy at the time of data cutoff. 4 re-induced patients are pending 6-month assessments.

A CR is defined as having a negative cystoscopy, a negative urine cytology, and a negative biopsy (as indicated).

Analysis based on both landmark CR rate assessed in clinical trial and DoR by Kaplan-Meier estimate.

The Role of DDM

DDM (n-dodecyl- β -D-maltoside) is an excipient administered alongside cretostimogene to enhance adenovirus delivery into tumor cells.



Temporary GAG disruption

DDM temporarily disrupts the glycosaminoglycan (GAG) layer of the bladder.¹



Improved penetration

This allows cretostimogene to more effectively penetrate tumor cells.¹

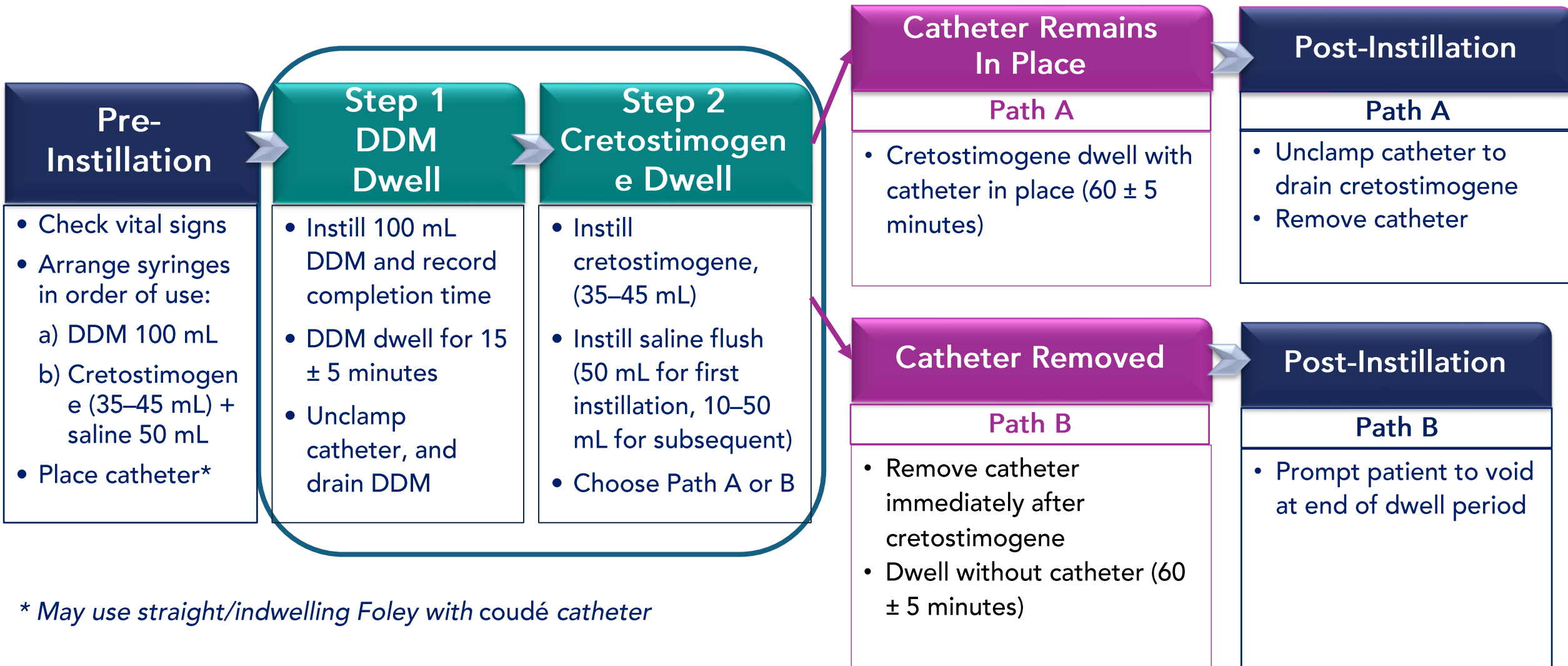


Preserved urothelium

Urothelium integrity is preserved; DDM showed favorable tolerability in preclinical studies.¹

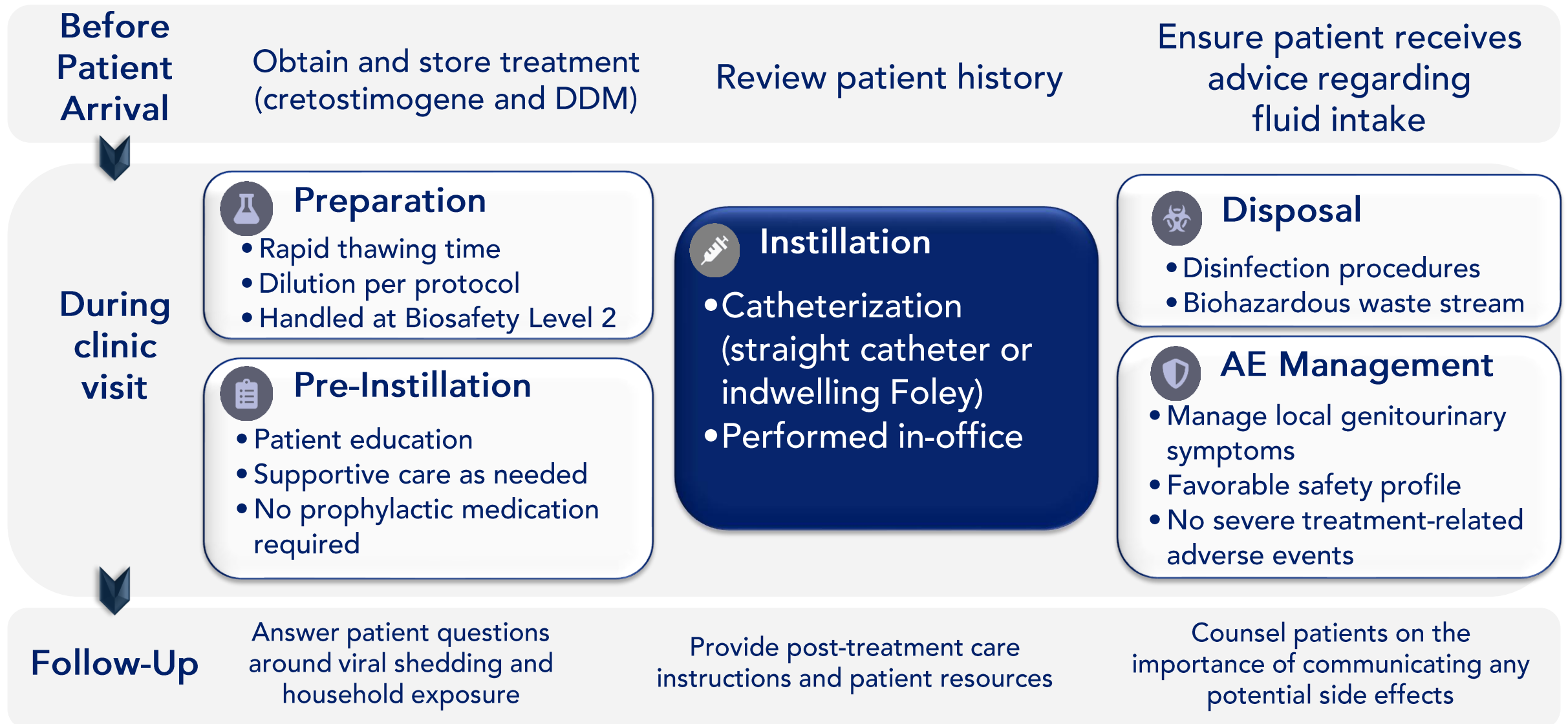
1. Ramesh et al., 2004

Cretostimogene and DDM 2-Step Instillation



* May use straight/indwelling Foley with coude catheter

The Cretostimogene Visit Workflow



Treatment-Emergent Adverse Events

Reported in <10% of BOND-003 C and CORE-008 A patients:

- Bladder spasm
- Dysuria
- Pollakiuria (frequency)
- Hematuria
- Fatigue*
- Urgency**

Patient Education

- Avoid fluid intake 4 hours before instillation
- Avoid bladder irritants

Other Techniques

- Supportive care (e.g., antispasmodics) may be administered before or after treatment if deemed necessary but **not required**
- Other measures can be implemented per provider order

Most treatment-related adverse events are mild to moderate and localized to the bladder.

Cretostimogene Follow-Up and Patient Education

For 7 days after treatment, patients should follow these precautions:



Hygiene

- Proper hand washing and housekeeping hygiene



Sexual Activity & Contraception

- Highly effective birth control and barrier methods must be used during sexual activity



Bathroom & Waste Precautions

- Minimize/avoid direct contact with urine
- Add bleach to toilet water
- Close lid before flushing
- Disinfect the seat



Close Contact with Others

- Close contact (kissing, hugging) is fine if symptom-free
- Avoid contact with others up to 2 weeks if febrile illness, respiratory symptoms, or diarrhea are present

What's next

xCEED: Phase 3 Combination Therapy for High-Risk BCG-Exposed NMIBC (CORE-008 Cohort E)

Key Eligibility Criteria

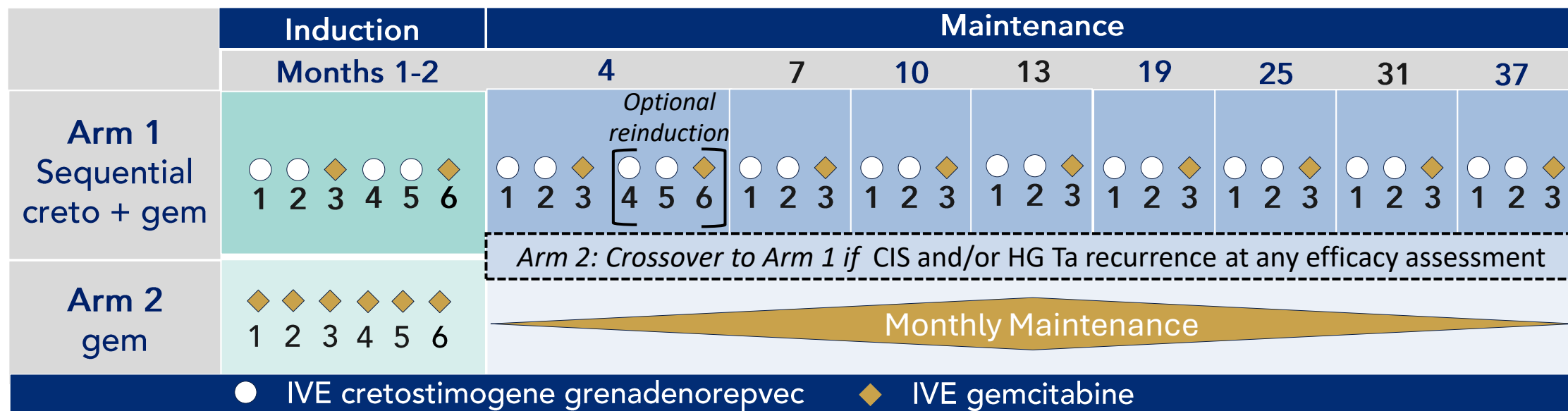
- HR BCG-Exposed NMIBC
 - CIS +/- Ta/T1 or HG T1/Ta
- No history of BCG-unresponsive NMIBC
- ECOG PS 0-2

Primary Endpoint

- EFS

Key Secondary Endpoints

- PFS
- CFS
- OS
- Safety
- DoR
- PROs



Reinduction is permitted in Arm 1 for biopsy-confirmed persistent high-grade Ta or CIS at the Month 3 efficacy assessment

BCG: bacillus Calmette-Guérin; CFS: cystectomy free survival; CIS: carcinoma in situ; creto: cretostimogene; DoR: duration of response; ECOG PS: Eastern Cooperative Oncology Group performance status; EFS: event-free survival; gem: gemcitabine; HG: high grade; HR: high risk; NMIBC: non-muscle invasive bladder cancer; OS: overall survival; PFS: progression free survival; PROs: patient reported outcomes

Summary & Conclusions

- Cretostimogene is an oncolytic immunotherapy with a dual MOA, demonstrating clinical efficacy and safety across BCG-unresponsive, BCG-exposed, and BCG-naive high-risk NMIBC populations
- Cretostimogene shows consistent efficacy and safety both as monotherapy^{*†}, in rational combination,[‡] and in an optimized 2-step administration,^{*} supporting its potential as a versatile backbone therapy across the NMIBC treatment continuum
- Easily fits within existing clinic workflow
- RNs and APPs are key to cretostimogene delivery, monitoring, and patient education
- Next: Phase 3 CORE-008 xCEED trial will evaluate cretostimogene combination therapy in high-risk BCG-exposed NMIBC

Cohort C; [†]CORE-008 Cohort A; [‡] CORE-008 Cohort CX

BCG: Bacillus Calmette-Guérin; CR: complete response; ITT: intent-to-treat; MIBC: muscle-invasive bladder cancer; MOA: mechanism of action; NMIBC: non-muscle invasive bladder cancer

THANK YOU QUESTIONS?



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