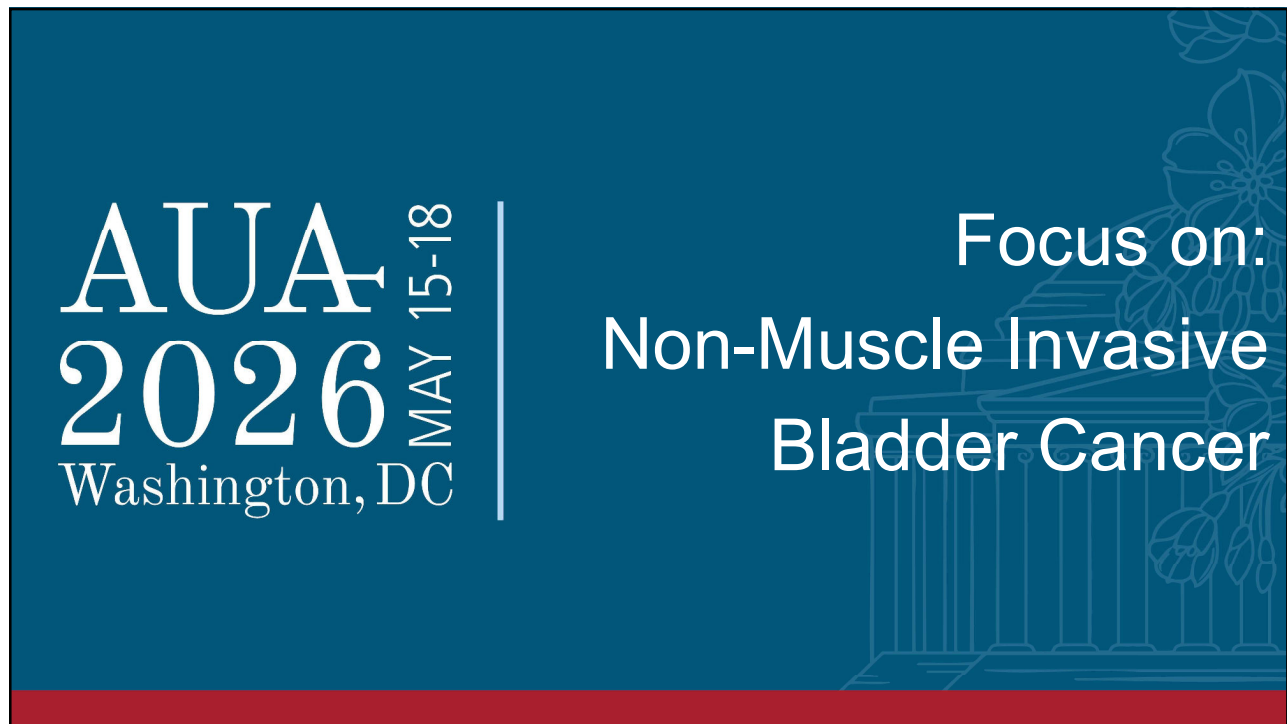




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AUA 2026
Washington, DC

MAY 15-18

Esteemed Colleagues

- Elizabeth Kessler
 - Medical Oncology: University of Colorado
- Suzanne Merrill
 - Community Urologic Oncology: Colorado Urology
- Mary Beth Westerman
 - Academic Urologic Oncology: UNC

2

In BCG-unresponsive CIS, what is your go-to?

- A. Nadofaragene
- B. Pembrolizumab
- C. Nogapendekin + BCG
- D. Clinical trial

3

What is your preferred treatment for Ta HG papillary-only recurrence:

- A. TAR-200
- B. Gem/Doce
- C. Early cystectomy
- D. Repeat BCG

4

For a healthy patient with recurrent CIS+TaHG who refuses cystectomy, what is your recommended next treatment?

- A. Pembrolizumab
- B. Intravesical therapy
- C. Trial
- D. Surveillance

5

- High-risk NMIBC has high recurrence and progression risk.
- BCG remains standard initial therapy.
- Cystectomy still has its role

6

- Variant (sarcomatoid, plasmacytoid, anaplastic, etc.)
- LVI
- Hydronephrosis

7

- BCG failure and shortages have driven innovation in intravesical and systemic therapies.

8

INTERMEDIATE RISK

9

Mitomycin reverse thermal gel

- Intermediate Risk-low grade
- ENVISION trial, FDA approved
- CR 79% (137/223) at 12 months

10

FDA APPROVED FOR CIS +/-TA/T1HG

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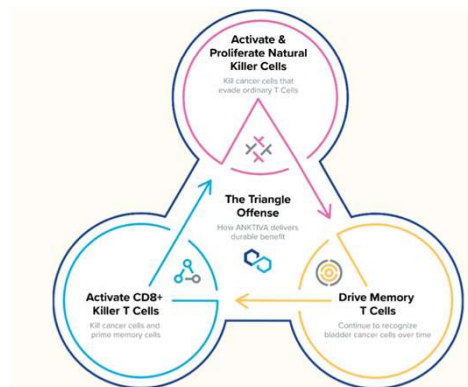
Nadofaragene Firadenovec

- Mechanism: Adenoviral IFN α gene therapy
- FDA Approved 2022, INSTILADRIN
- CR ~30% at 36 months



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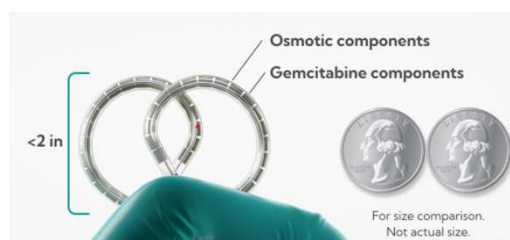
- Mechanism: IL-15 agonist
- FDA Approved, Quilt-3.032
- Enhances immune activation with BCG
- CR 40% at 24months (N=19/77)



FDA package insert

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- Mechanism: Sustained gemcitabine delivery
- FDA Approved 2025, SUNRISE-1
- CR 51% (N=35/83) at 12 months



14

- Mechanism: Cytotoxic chemotherapy
- Not FDA approved combo
- Strong real-world outcomes
- CR ~40% at 2 years

15

Summary of 12-Month Outcomes

Favors BST	No Difference	Favors RC
Bowel health Sexual health	Physical functioning • Overall • By age Role functioning Social functioning Urinary health	Physical functioning • Patients w/ CIS • Unpartnered Cognitive functioning Mental health Financial health
Progression-free survival	Cancer-specific survival Overall survival	Recurrence-free survival

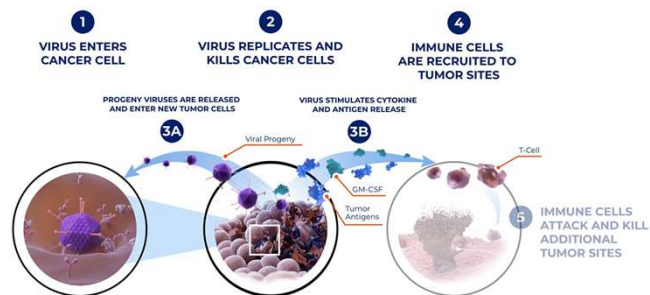
16

ONGOING TRIALS OR WITH THE FDA

17

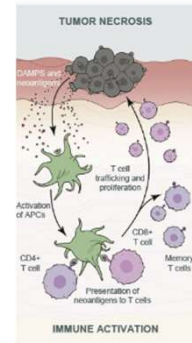
Cretostimogene

- Mechanism: Oncolytic virus + GM-CSF
- Fast Track
- CR ~75%



18

- Mechanism: Light-activated VDC
- Investigational
- Localized tumor destruction



19

- BCG Unresponsive CIS
- LEGEND trial, Phase II
- Non-viral genetic, localized gene therapy

20

- Sustained release gem/docetaxel, release up to 10 days
- Phase III
- Intermediate risk NMIBC, BOOST trial

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SYSTEMIC THERAPIES FOR HR NMIBC

22

- Mechanism: PD-1 inhibitor
- FDA Approved 2020, KEYNOTE-057
- Systemic option for BCG-unresponsive CIS

23

- Mechanism: PD-L1 inhibitor
- No new safety outcomes, POTOMAC

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Controversy: Best First Salvage?

- Nadofaragene vs Pembrolizumab vs BCG+nogapendekin
- No head-to-head trials
- Decision driven by patient + toxicity + logistics

25

Treatment Sequencing

- No clear algorithm
- BCG reinduction thing of the past?
- Requires individualized decision-making

26

- Systemic: broader immune activation
- Intravesical: lower toxicity
- Patient selection critical

27

- Many therapies single-arm
- Trials guide future standards

28

65M, T1HG + CIS

Question: What is first-line therapy?

- A. BCG induction
- B. Pembrolizumab
- C. TAR-200
- D. Cystectomy

29

- Answer: BCG induction
- Pearl: BCG remains first-line for HR-NMIBC; early adequate induction is critical.

30

92F persistent CIS after BCG

Question: Best next treatment option?

- A. Nadofaragene
- B. Repeat BCG
- C. Surveillance
- D. TURBT only

31

- Answer: Nadofaragene firadenovec
- Pearl: Gene therapy with q3 month dosing.

32

68M BCG-unresponsive CIS + TaHG

Question: Preferred approach?

- A. Nogapendekin + BCG
- B. Radiation
- C. Antibiotics
- D. Observation

33

- Answer: nogapendekin + BCG
- Pearl: Combination immunotherapy enhances response in CIS-containing disease.

34

75M BCG-unresponsive, refuses surgery

Question: Best systemic option?

- A. Pembrolizumab
- B. BCG reinduction
- C. TURBT alone
- D. None

35

- Answer: Pembrolizumab
- Pearl: Systemic therapy reserved for cystectomy-ineligible or refusing patients.

36

70F heart failure and 4L oxygen baseline, CIS+TaHG papillary-only recurrence after BCG

Question: Best therapy?

- A. TAR-200
- B. Cystectomy immediately
- C. Radiation
- D. Surveillance

37

- Answer: TAR-200
- Pearl: Sustained drug delivery improves exposure and convenience.

38

60M multiple TaHG recurrences post-BCG

Question: Reasonable salvage?

- A. Gem/Doce
- B. TURP
- C. Antibiotics
- D. None

39

- Answer: Gemcitabine/Docetaxel
- Pearl: Widely used salvage with strong retrospective efficacy.

40

66F fit, BCG-unresponsive CIS

Question: Best approach?

- A. Trial
- B. Do nothing
- C. Repeat TURBT only
- D. Radiation

41

- Answer: Clinical trial
- Pearl: Trials are critical given evolving landscape and lack of sequencing clarity.

42

Controversy: When to Cystectomy?

- Early cystectomy improves oncologic control
- But overtreatment risk
- Balance biology vs patient preference

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Algorithm for HR-NMIBC

1. BCG-NAÏVE HIGH-RISK
→ Full-dose BCG induction + maintenance
2. BCG-UNRESPONSIVE, CIS ± papillary:
→ Nadofaragene OR nogapenedekin + BCG OR TAR-200 OR gem/doce
→ Consider Pembrolizumab if systemic candidate
3. HIGH-RISK FEATURES (T1HG, LVI, variant)
→ Early cystectomy discussion
4. THROUGHOUT ALL STAGES
→ Clinical trial prioritization
5. PRINCIPLE
→ No fixed sequencing → personalize based on biology + patient goals

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- NMIBC landscape rapidly evolving
- Multiple FDA-approved options now available
- No defined sequencing strategy
- Shared decision-making is essential
- Clinical trials remain critical