A Land with Only Limited Access to BCG - Treatment Options for NMIBC

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Objectives:

- Review scope of BCG shortage
- Risk Stratify NMIBC effectively
- Select appropriate alternative treatment options for NMIBC
- Review updated guideline-driven protocols
- Provide practical treatment algorithms

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NMIBC Background

- 85,000 new cases of bladder cancer expected in 2026
- Approximately 75% of patients present with localized, non-muscle invasive bladder cancer (NMIBC)
- The current standard of care for intermediate and high-risk NMIBC
  - resection of all visible disease
  - induction intravesical treatment with BCG and then maintenance therapy for 1 to 3 years

- **Prospective data have supported the first-line use of BCG for over 20 years**

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Why BCG shortage matters..

BCG = gold standard for intermediate/high risk NMIBC

Proven decreased recurrence and progression

Shortage forces deviation from standard care

Clinical + ethical implications

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Scope of the BCG shortage

Ongoing since ~ 2012

Limited manufacturing capacity

Single major supplier (Merck & Co.)

Demand exceeds supply globally

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AUA Guidelines Principles

1. Prioritize high-risk patients
2. Use reduced dosing strategies
3. Limit maintenance therapy
4. Avoid BCG in low-risk disease (not new)

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AUA Risk Stratification for NMIBC

Low Risk	Intermediate Risk	High Risk
LG [a] solitary Ta ≤ 3cm	Recurrence within 1 year, LG Ta	HG T1
PUNLMP [b]	Solitary LG Ta > 3cm	Any recurrent, HG Ta
	LG Ta, multifocal	HG Ta, >3cm (or multifocal)
	HG [c] Ta, ≤ 3cm	Any CIS [d]
	LG T1	Any BCG failure in HG patient
		Any variant histology
		Any LVI [e]
		Any HG prostatic urethral involvement

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Risk Stratification Refresher

Low-risk: LG Ta

Intermediate-risk: recurrent LG, multifocal, LG T1

High-risk: HG Ta, T1, and CIS, variant histology, LVI, prostatic involvement

Drives treatment decisions during shortage

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Standard BCG Protocol (Pre-Shortage)

- Induction: 6 weekly instillations
- Maintenance: SWOG protocol (3 years)
- Proven survival benefit

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Key Protocol Changes

- Full-dose → 1/2 – 1/3 dose BCG
- Maintenance shortened to 1 year or less
- Prioritization of induction over maintenance

Why is BCG dose reduction used during shortage…

- Limited supply → maximize patient access
- Evidence supports reduced dosing (1/2-1/3 dose)
- Immune mechanism does not require full dose
- Prioritize induction over maintenance
- Risk stratified allocation
- Avoid delays or inferior alternatives
- Improved tolerability may enhance completion

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Clinical trial data..

"A recent study looked at 563 patients with NMIBC treated with adequate BCG, 150 patients received 1/3 dose and 413 received full dose BCG. The use of 1/3 dose BCG did not adversely affect time to recurrence or time to progression. When stratified by 2021 EA prognostic factor risk group, 1/3 dose BCG was not associated with worse time to progression. **Cancer specific survival was similar between patients receiving 1/3 dose and full dose BCG" (Lobo et al, 2025)**

Dose Reduction Evidence

- Trials show similar oncologic outcomes
- Reduced toxicity
- Widely adopted during shortage

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Who Gets BCG First

- Highest priority:
  - T1 high-grade
  - CIS
  - Early Recurrence HG
- Lower priority
  - Intermediate-risk
  - Maintenance patients

Case Scenario:

68-year-old male

Gross hematuria → TURBT

Pathology: T1 high grade urothelial carcinoma

No CIS identified

Re resection negative

No BCG available for 6-8 weeks

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Options…

1. Wait for BCG

2. Start alternative therapy
   - Gem/Doce increasingly used
   - Very reasonable if delay uncertain

3. Early Cystectomy discussion
   - Especially if
     - LVI
     - Variant histology
     - High-volume T1

Take Home Message

- Don't default to waiting
- Have a defined backup plan
- Start counseling on cystectomy early

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Intermediate Risk NMIBC Strategy

Intravesical chemotherapy preferred:

- Gemcitabine
- Mitomycin
- Valrubicin
- Gemcitabine/Docetaxel

Consider induction + Maintenance chemotherapy

Case Scenario

- 72-year-old female
- History: LG Ta bladder cancer
- Now with multifocal recurrence
- Prior single dose gemcitabine only
- Asking: “Do I need BCG now?”

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This is intermediate-risk disease

During shortage → NO BCG

Intravesical approach:
- -Gemcitabine
- -Mitomycin C
- -Gem/Doce

Why?
- Excellent recurrence control
- Lower toxicity
- Preserves BCG supply

High-Risk NMIBC Without BCG

Consider:

- Early Cystectomy
- Intravesical chemo regimens
- Clinical trials

Shared decision-making critical

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Radical Cystectomy Considerations

- Gold Standard for highest risk disease
- Underutilized in delayed BCG access
- Improved survival when done early

Systemic Immunotherapy

- Pembrolizumab (Keytruda)
- FDA approved for BCG unresponsive CIS
- IV therapy Q3-6 weeks
- Monitor immune related adverse events

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Gene Therapy: Nadofaragene Firadenovac (Adstilladrin)

- Intravesical viral vector therapy
- Given every 3 months
- Durable responses in CIS

Novel Immunotherapy
Nogapendekin alfa inbakicept (Anktiva)

- IL - 15 superagonist + BCG backbone
- Option with partial BCG available

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TAR – 200 drug delivery system (Inlexzo)

Slow-release continuous Gemcitabine pretzel stent

Manufacturer image

Single-Dose Post TURBT Chemo

- Gemcitabine immediately post op
- Decrease recurrence risk significantly
- Underutilized high-impact intervention

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Case Scenario

65-year-old male
CIS after induction + maintenance BCG
Persistent positive cytology
Refuses cystectomy
Good performance status

This is BCG unresponsive disease & patient refused cystectomy….

Options:

1. Pembrolizumab
2. Nadofaragene Firadenoec
3. Nogapendekin alfa inbackicept (if BCG available)
4. Gem/Doce
5. TAR 200

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Practical Clinic Workflow Changes

- BCG allocation tracking system
- Prioritization protocols
- Pharmacy coordination
- Patient counseling standardization

Patient Counseling

- Explain shortage transparently
- Discuss alternative efficacy
- Address anxiety about deviation from “gold standard”
- Emphasize close surveillance

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Proposed Treatment Algorithm

- High-risk:
  - BCG (reduced dose) → if unavailable → gem doce or cystectomy
- Intermediate-risk:
  - Intravesical chemo first line
- Low Risk
  - TURBT +/- single-dose chemo

Key Takeaways

- BCG Shortage = long term reality
- Risk-stratification is essential
- Intravesical chemo is highly effective
- New therapies expanding options
- Early cystectomy should not be delayed

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