PRACTICE AID

Adverse Event Management Approaches in Bladder Cancer

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/Bladder2024**

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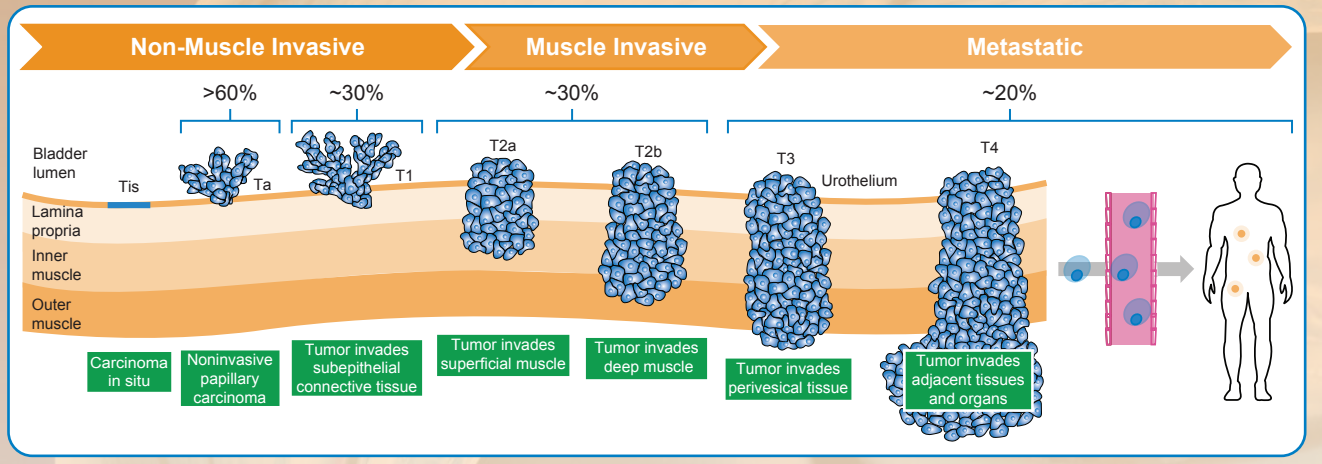
FGFR Alterations Are Frequently Observed in Bladder Cancer[1,2]



Eligibility for FGFR inhibition requires testing for genomic alterations

- ❑ Patients ideally undergo testing upon diagnosis
- ❑ Options include specifically testing tumors for *FGFR3* alterations (eg, RT-PCR companion assay) or more comprehensive approaches (eg, NGS panels, liquid biopsy)
- ❑ Urologists have an important role in educating patients on the implications of genomic testing

Erdafinitib: Understanding Safety Considerations[3,4]

General Guidance on AEs Associated With FGFR3 Inhibitors

- FGFR3 inhibitors are associated with unique AEs
- Oral hygiene is critical; mucositis and other oral toxicities can be a concern
- Monitor for skin and nail toxicities, referring to dermatology and podiatry as needed
- Close monitoring and supportive care is important

Hyperphosphatemia

- Erdafitinib also inhibits FGFR signaling in the proximal renal tubule, impairing function of the sodium-dependent phosphate co-transporter
- Dietary phosphate may require restriction
  - Consult a nutrition professional (eg, registered dietitian, nutritionist) for individualized dietary planning
  - Consider adding a non–calcium-containing phosphate binder (eg, sevelamer carbonate)

Ocular Toxicities

- Recommended ophthalmologic examinations
  - Monthly for first 4 mo; every 3 mo thereafter
  - At any time for visual symptoms
- For any occurrence of central serous retinopathy (CSR)/retinal pigment epithelial detachment (RPED):
  - Withhold erdafitinib; discontinue permanently if symptoms do not resolve in 4 wk
  - Discontinue permanently for grade 4 CSR/RPED

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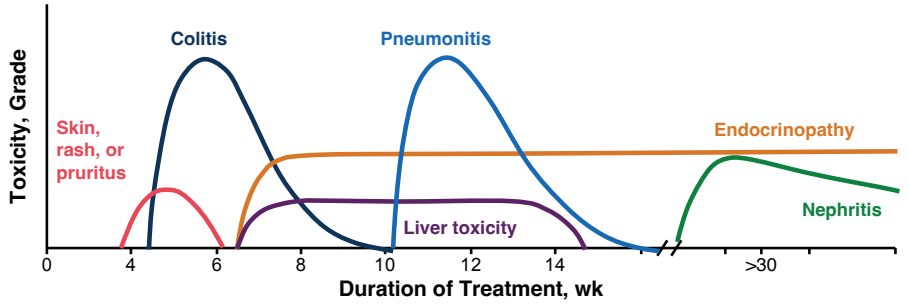
Counseling Patients on irAEs Associated With Immune Checkpoint Inhibitors[5-8]

irAEs Can Affect Any Organ System …

Dermatologic	Gastrointestinal	Endocrine	Pulmonary
• Rash • Pruritus	• Diarrhea • Nausea/Vomiting • Hepatitis	• Hypothyroidism	• Pneumonitis

… And the Timing of Events Is Variable



Patient education must focus on the importance of prompt recognition and management of irAEs

irAE Grading and Management: Overall

Grade 1

Minimal or no symptoms; diagnostic change only

- In general, immune checkpoint inhibitor therapy should be continued with close monitoring, with the exception of some neurologic, hematologic, and cardiac toxicities

Grade 2

Mild to moderate symptoms

- Hold checkpoint inhibitor therapy for most grade 2 toxicities
- Consider resuming immunotherapy when symptoms and/or laboratory values revert to grade 1 or lower
- Corticosteroids (initial dose of 0.1-1 mg/kg/d of prednisone or equivalent) may be administered

Grade 3/4

Severe or life-threatening symptoms

Grade 3

- Hold checkpoint inhibitor therapy
- Initiate high-dose corticosteroids (prednisone 1-2 mg/kg/d or methylprednisolone IV 1-2 mg/kg/d)
- If symptoms do not improve with 48-72 h of high-dose corticosteroids, infliximab may be offered for some toxicities
- Taper corticosteroids over the course of at least 4-6 wk
- When symptoms and/or laboratory values revert to grade 1 or lower, rechallenging with immunotherapy may be offered; however, caution is advised, especially in those patients with early-onset irAEs; dose adjustments are not recommended

Grade 4

- In general, permanent discontinuation of checkpoint inhibitor therapy is warranted, with the exception of endocrinopathies that have been controlled by hormone replacement

1. Knowles MA et al. *Nat Rev Cancer*. 2015;15:25-41. 2. Nimgaonkar N et al. *JAMA Oncol*. 2022;8:1070-1072. 3. Loriot Y et al. *N Engl J Med*. 2019;381:338-348. 4. Siefker-Radtke AO et al. *Lancet Oncol*. 2022;23:248-258. 5. Martins F et al. *Nat Rev Clin Oncol*. 2019;16:563. 6. Postow MA et al. *N Engl J Med*. 2018;378:158-168. 7. Schneider BJ et al. *J Clin Oncol*. 2021;39:4073-4126. 8. NCCN Clinical Practice Guidelines in Oncology. Management of Immunotherapy-Related Toxicities. Version 1.2024. https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf.

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Expanding Role of Therapeutic Approaches in Bladder Cancer

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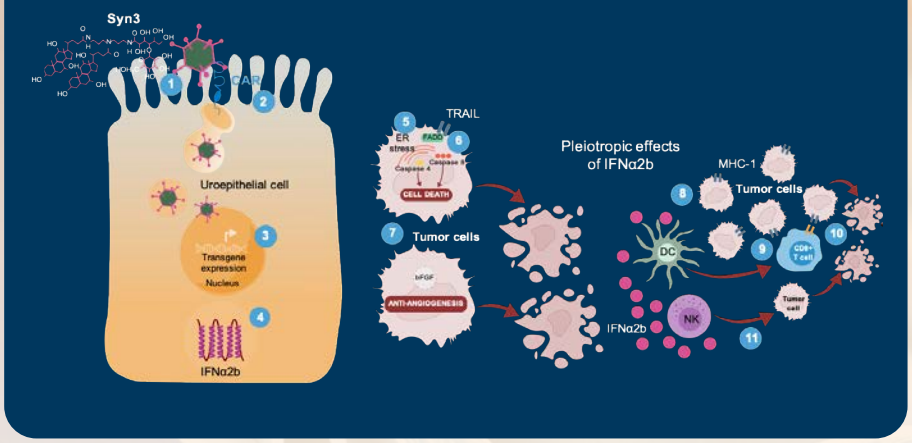
Treatment Approaches for NMIBC[1]

Pembrolizumab

FDA-approved checkpoint inhibitor for the treatment of patients with BCG-unresponsive, high-risk NMIBC with carcinoma in situ with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy based on the KEYNOTE-057 trial[2]

Nadofaragene firadenovec is a nonreplicating adenoviral vector–based gene therapy that delivers human *IFNα2b* cDNA to urothelial cells and Syn3 to enhance viral transduction of the urothelium. *IFNα2b* cDNA is transcribed into IFNα2b protein in bladder epithelial cells, where it inhibits tumor growth

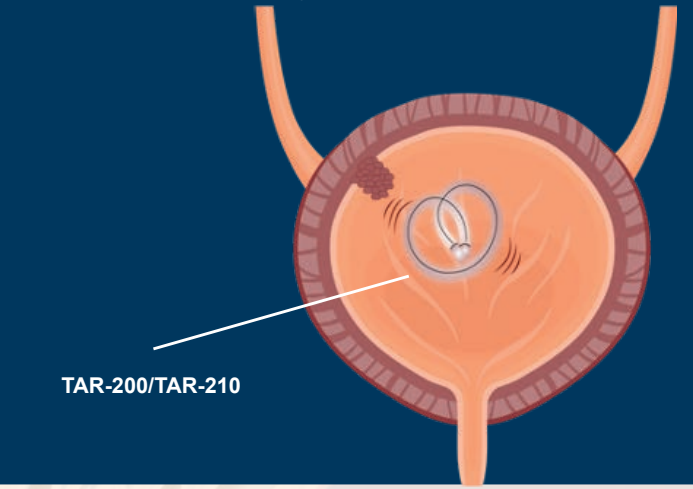


Nadofaragene firadenovec is the first gene therapy approved by the FDA for the treatment of adult patients with BCG-unresponsive, high-risk NMIBC with CIS with or without papillary tumors based on the phase 3 ADSTILADRIN trial.

Clinical Trials Assessing Nadofaragene Firadenovec

- **Phase 4 ABLE-41:** real-world evidence study of patients being treated with nadofaragene firadenovec in a US-based routine clinical setting (BCG-unresponsive high-risk NMIBC)
- **Phase 2 ABLE-22:** nadofaragene firadenovec ± chemotherapy or pembrolizumab (BCG-unresponsive high-risk NMIBC)
- **Phase 3b ABLE-32:** nadofaragene firadenovec vs observation (intermediate-risk NMIBC)
- **Phase 4 ABLE-42:** retreatment with nadofaragene firadenovec (high-grade BCG-unresponsive NMIBC)

Intravesical drug delivery system that enables a sustained release of gemcitabine (TAR-200) or erdafitinib (TAR-210) into the bladder, increasing the dwell time of the local drug concentration



Clinical Trials Testing Intravesical Approaches

- **Phase 2 SunRISe-1:** TAR-200 in BCG-unresponsive NMIBC
- **Phase 2 SunRISe-3:** TAR-200 in BCG-naïve NMIBC
- **Phase 3 SunRISe-5:** TAR-200 vs intravesical chemo in BCG-unresponsive NMIBC
- **Phase 1 TAR-210:** high-risk or intermediate-risk NMIBC with *FGFR* alterations
- **Phase 3 MoonRISe-1:** TAR-210 vs IV chemo in intermediate-risk NMIBC with *FGFR* alterations

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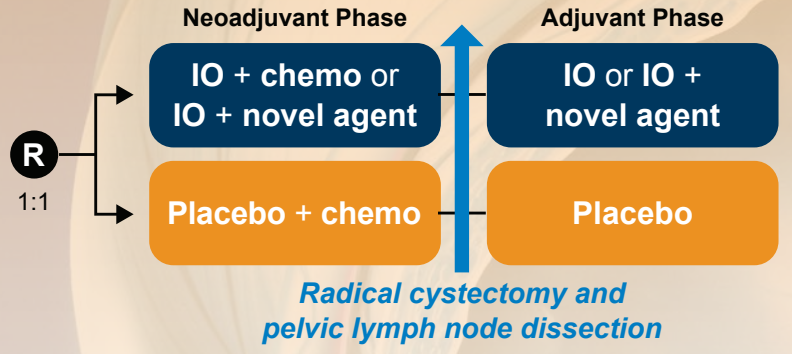
Approaches for MIBC[1]

Nivolumab
FDA approved for the adjuvant treatment of patients with MIBC who are at high risk of recurrence after undergoing radical resection (phase 3 CheckMate -274)

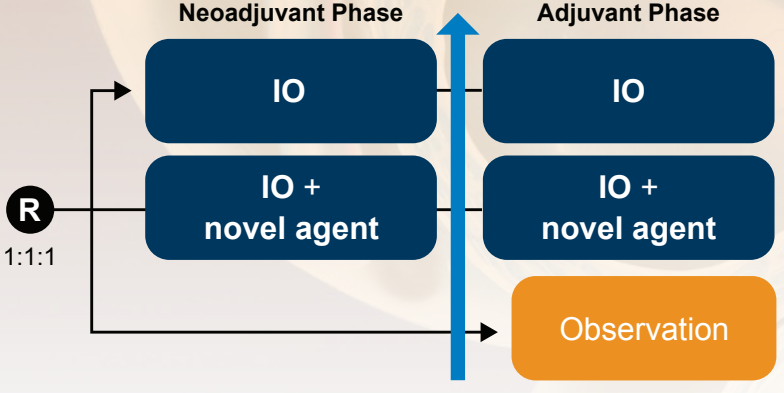
Cisplatin Eligible



Cisplatin-Eligible Trials

- **Phase 3 CA017-078:** gem/cis ± nivolumab (fully accrued N = 861)
- **Phase 3 NIAGARA:** gem/cis ± durvalumab (fully accrued N = 1,063)
- **Phase 3 KEYNOTE-866:** gem/cis + pembrolizumab (fully accrued N = 907)
- **Phase 3 KEYNOTE-B15/EV-304:** pembrolizumab + EV

Cisplatin Ineligible



Cisplatin-Ineligable Trials

- **Phase 3 KEYNOTE-905/EV-303:** pembrolizumab + EV
- **Phase 3 VOLGA:** durvalumab + tremelimumab + EV
- **Phase 2 SunRISe-4:** TAR-200 + cetrelimab

Approaches for Unresectable or mUC[1]

FDA Approved in the First-Line Setting

- **Nivolumab + gem/cis** (phase 3 CheckMate -901)
- **Enfortumab vedotin + pembrolizumab** (phase 3 EV-302)

FDA Approved in the Second-Line Setting

- **Erdafitinib in mUC with select *FGFR3* alterations** (phase 3 THOR)
- **Sacituzumab govitecan** (phase 2 TROPHY-U-01)
- **Trastuzumab deruxtecan (T-DXd) in HER2+/IHC3+ mUC** (phase 2 DESTINY-PanTumor02)

1. clinicaltrials.gov. 2. Balar AV et al. *Lancet Oncol*. 2021;22:919-930.

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Patient Resources for Healthcare Professionals[1]

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BCAN Bladder Cancer Advocacy Network

Leading the way to awareness and a cure

The Bladder Cancer Advocacy Network (BCAN) is a national advocacy organization that is committed to advancing bladder cancer research and supporting those impacted by the disease.

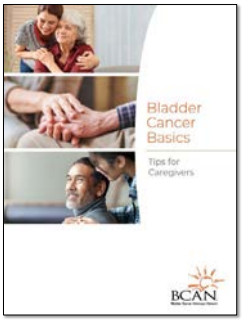
FREE BLADDER CANCER PATIENT RESOURCES FOR HEALTHCARE PROVIDERS

BCAN Bladder Cancer Advocacy Network

Get Yours Today!

BCAN provides free online and printed educational resources designed to help patients, caregivers, and the medical community learn about bladder cancer and treatment options.

- **Printed materials**
- **Patient videos**
- **Webinars**
- **Podcasts**
- **Treatment matrix**
- **Clinical trials dashboard**
- **Bladder cancer support line: 833-ASK-4-BCA**



1. https://bcan.org.