Operationalizing a Breakthrough Bladder Cancer Medication With a Multidisciplinary Approach:

Insights From Nurse Leaders

sorbetto - Getty Images

BY REBECCA FARRELL, MSN, RN, NEA-BC, AND
ERIN LONGSTRETH-PAPSUN, MSN, RN, OCN, NEA-BC

Non–muscle-invasive bladder cancer is one of the most common forms of bladder cancer in the United States. Roughly 75% of bladder cancer cases are classified as non–muscle-invasive at diagnosis.[1] According to the American Cancer Society, bladder cancer is the fourth most common cancer in the US, with an estimated 83,190 new cases diagnosed in 2023 (about 63,070 in men and 20,120 in women).[2]

While non–muscle-invasive bladder cancer has a better prognosis compared to muscle-invasive bladder cancer, it often requires long-term follow-up due to its high recurrence risk, ranging from 50% to 70%.[1] The 5-year survival rate for this type of cancer is around 96%, depending on the stage and grade of the tumor.[2] The high incidence and recurrence of non–muscle-invasive bladder cancer make it a significant concern in public health and long-term management.

Treatment of non–muscle-invasive bladder cancer is rapidly evolving, with novel therapies offering hope for better outcomes, especially for patients who fail standard treatments like Bacillus Calmette-Guérin. The most promising new treatments include immune checkpoint inhibitors, vaccine-based therapy, intravesical chemotherapy, targeted therapy with fibroblast growth factor receptor inhibitors, and combination therapies.[1] The landscape of treatment is becoming more tailored, with a focus on immunotherapy, gene therapy, and precision medicine. These treatments are critical for patients who do not respond to Bacillus Calmette-Guérin, as they offer bladder-preserving alternatives to radical cystectomy.

A New Therapy

Nadofaragene firadenovec (Adstiladrin®) is a novel approach to treating non–muscle-invasive bladder cancer that is unresponsive to traditional therapies like Bacillus Calmette-Guérin.[3] This gene therapy is unique when compared to conventional chemotherapy or immunotherapy. According to Boorjian et al, this therapy uses a modified adenovirus to deliver the gene for interferon alfa-2b, a protein that has antitumor effects.[4] Once delivered into the bladder cells, the body produces elevated levels of interferon locally, enhancing the immune response against cancer. The gene therapy has shown high efficacy in this difficult-to-treat group. Phase 3 clinical trial data reported a 53.4% complete response rate at 3 months after the first dose, and 45.5% of the complete responders continue to have a complete response at 12 months.[4] This medication is offering hope to patients whose other treatments have failed.

> Nurse leaders use the nursing process to ensure any new initiative is safe, effective, and patient-centered.

Compared to systemic chemotherapy or even some immunotherapies, this treatment is well tolerated. Since the drug is delivered directly into the bladder, it minimizes systemic adverse effects, allowing patients to maintain a better quality of life during treatment. The interferon gene introduced by nadofaragene firadenovec continues to stimulate the body's immune response over time, making it potentially more durable when compared with other medications that require more frequent administration or have shorter-lasting effects.[4] Approved by the Food and Drug Administration (FDA) in 2022, this gene therapy was not made commercially available until January 2023, allowing health care facilities with the highest number of appropriate patients with non–muscle-invasive bladder cancer to apply for an Early Experience Program. If accepted to this program, facilities can treat as many patients as possible in the short term while ensuring that every patient who started treatment could continue on the therapy for the duration of their prescribed treatment.

A Multidisciplinary Approach to Operationalizing This New Treatment

Fox Chase Cancer Center, part of the Temple University Health System, is a National Cancer Institute (NCI)–designated comprehensive cancer center in Philadelphia, Pennsylvania, and a leader in urologic oncology, offering cutting-edge therapies for patients with bladder cancer. After applying to the drug manufacturer's Early Experience Program, Fox Chase was chosen to begin treating patients with non–muscle-invasive bladder cancer with this innovative treatment option before it became widely available.

Figure 1. Interdisciplinary Steering Committee

While nurse leaders play a pivotal role during any new process implementation, these professionals are rarely included in the implementation of new drug therapies. Interdisciplinary collaboration is a complex process that is necessary for new drug therapies. Nurse leaders use the nursing process to ensure any new initiative is safe, effective, and patient-centered. At Fox Chase Cancer Center, genitourinary service line leaders, pharmacy representation, clinical nurse leaders, financial counselors, and urologic oncologists helped to operationalize this new treatment; this group formed the Adstiladrin Steering Committee (**Figure 1**).

Implementation Process

The steering committee identified the following 8 steps that are needed before implementation occurs:

1. Confirmation that the medication is FDA approved
2. Hospital formulary review and approval
3. Pharmacy preparation and support
4. Logistics and supply chain management
5. Insurance and reimbursement verification
6. Education and consent
7. A process to monitor and report on patients prescribed this treatment
8. Multidisciplinary collaboration

Step 1. Confirmation of FDA Approval

Nadofaragene firadenovec was approved by the FDA in 2022, so institutional review board approval was not needed. Instead, the steering committee consulted the biosafety officer in the research safety department to perform a biosafety review as due diligence to ensure the necessary precautions were in place for the safety of patients, staff, and the institution. To receive full biosafety approval, the clinical nurse leader drafted a standard of practice, clinical education, and patient education based on the FDA drug insert information and presented it to the biosafety officer. Once approval was received, the team moved on to the next step.

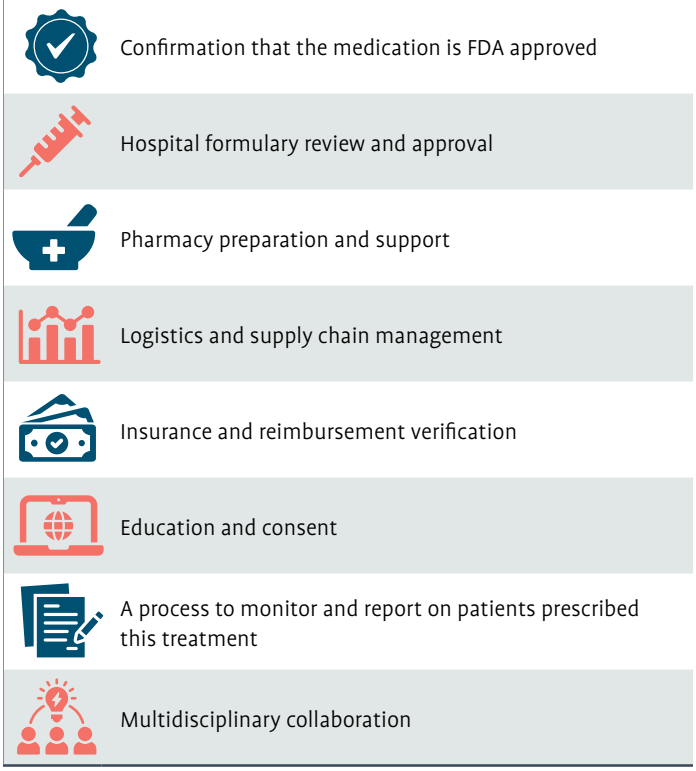
Step 2. Hospital Formulary Review and Approval

Nadofaragene firadenovec was presented to the Pharmacy and Therapeutics (P&T) Committee to evaluate whether the drug should be added to the hospital's formulary. The committee reviewed the clinical data, cost-effectiveness, safety profile, and the hospital's capacity to administer the treatment. Given that Fox Chase has an expansive intravesical treatment clinic in its Department of Urology, the committee decided that this novel treatment would be administered there instead of in the outpatient infusion room. A cost-benefit analysis performed by the P&T committee reviewed the cost of the medication, potential reimbursement, and the availability of funding or subsidies. Once the P&T committee received approval, the secretary of the committee created a supportive plan order in the electronic health record (EHR), with all the required information for the drug to be ordered, and created electronic consent.

Step 3. Pharmacy Preparation, Informed Consent, and Support

Although proficient in the preparation of other intravesical medications, nadofaragene firadenovec-specific education was required before treating the first patient. As this drug is a nonreplicating adenovirus, drug preparation precautions were implemented and reviewed with all pharmacy staff.

FIGURE 2. IMPLEMENTATION PROCESS



There are significant compounding and storage requirements for this gene therapy. The drug is shipped in an insulated container and must be frozen until ready for use. Once thawed, vials are stored at room temperature or refrigerated for up to 24 hours before use. When nadofaragene firadenovec was first offered, the medication needed to be administered within 1 hour of preparation, which necessitated careful planning by the multidisciplinary team. Fortunately, as of July 2024, the FDA updated the viability time to 6 hours once the medication is drawn into the syringe.

Step 4. Logistics and Supply Chain Management

As a member of the Early Experience Program, patients were guaranteed a dose of nadofaragene firadenovec for the duration of their prescribed treatment. The treatment is administered once every 3 months, so the enrolled patients will receive treatment for as long as their response to therapy is favorable.

The Department of Urology is in a network location that is a half mile from the main campus of Fox Chase and the pharmacy. Since the viability of the medication was initially 1 hour, nursing and pharmacy teams created the following steps to ensure the medication was delivered on time and well within the viability time:

- Patients were told to arrive 1 hour before their appointment.
- The indwelling catheter was inserted, premedication was administered, and education was reviewed with the patient.
- Next, the nurse would send the pharmacy a message using the chat feature of the EHR confirming the patient was ready, which alerted the pharmacy to call the hospital courier to pick up the medication for delivery.
- The pharmacy team would draw the medication into the syringes and the countdown began.
- Once the medication was delivered, the administering nurse began the instillation.

Once the viability increased to 6 hours, the process of compounding and medication delivery was much easier.

Step 5. Insurance and Reimbursement Verification

The hospital's billing department was engaged early in the planning process. The finance team must ensure that payers will cover the new medication because it is very costly. This step may include negotiating reimbursement rates with public and private payers. When a patient is identified as eligible for treatment with nadofaragene firadenovec, the ordering provider or registered nurse notifies the financial navigation team. Once the patient is financially approved, the financial navigation team will notify genitourinary leadership and the pharmacy to order the medication from the manufacturer. Without this key step, appointment scheduling and treatment are delayed.

Step 6. Education and Consent

All patients who are prescribed this medication have had prior intravesical treatment, so the primary focus of the patient education is on the medication, adverse effects, premedications, and what to expect on the day of treatment. The nurse leader created education for the clinical staff using the FDA package insert, a brochure from the drug manufacturer, and recommendations from the biosafety officer. Patient education begins when the provider suggests treatment with the gene therapy and is ongoing. Once the provider obtains informed consent, the nurse will begin the education both verbally and with written handouts.

Nurse leaders ensure that nursing staff and other health care professionals are well-educated about any new therapy, including administration, adverse effects, contraindications, and patient management. These professionals organize training sessions, provide resources, and clarify treatment and medication protocols. What's more, nurse leaders help develop and implement clinical practice guidelines and policies for new drugs. These responsibilities include creating protocols for patient monitoring, handling adverse reactions, and managing the coordination of drug administration.

> When professionals with diverse expertise come together, they contribute different ideas and knowledge, which leads to more informed, well-rounded decisions.

Step 7. A Process to Monitor and Report on Patients Prescribed This Treatment

Hospitals have protocols for ongoing monitoring of patients receiving new cancer treatments, which could include regular lab tests, imaging, or follow-up visits to assess efficacy and adverse effects. Because Fox Chase was a part of the Early Experience Program, every patient was tracked using a secure shared document mapping out financial clearance, appointment scheduling, referring provider, treatment schedule, adverse reactions, posttreatment urine cytology results, and cystoscopy findings.

Adverse reactions or unexpected outcomes must be reported to regulatory agencies like the FDA and the pharmaceutical company (manufacturer) for ongoing safety evaluation. Although no adverse reactions were observed in the first 6 patients at Fox Chase Cancer Center, the 1 common issue identified was bladder spasms. Patients were premedicated with an anticholinergic medication 1 hour before instillation; however, this precaution did not prevent or reduce bladder spasms. Pharmacy, genitourinary leadership, and nursing staff reevaluated the indications for the medication and found that the maximum benefit for spasm prevention was to take the medication 4 to 6 hours before the instillation. This change was immediately made, but given the severity of the spasms, the team modified the protocol, so the patient began taking the medications 3 days before the appointment. Bladder spasms were less severe, but not eliminated. This process and the modifications were documented and tracked.

Step 8. Multidisciplinary Collaboration

During planning and implementation, in addition to genitourinary leadership, the nurse leader collaborated often with physicians, pharmacists, and other members of the multidisciplinary team to maintain a coordinated approach to planning and implementation. Nurse leaders promote communication and problem-solving across disciplines to optimize patient outcomes. Their responsibilities include monitoring for adverse events, reviewing documentation, and conducting quality improvement audits, as needed.

Regular team meetings were scheduled to review the process and provide updates. Changes were made based on patient experiences and identified areas of process improvement. Objectives were frequently reviewed to ensure milestones were being achieved. When milestones were achieved, each success was celebrated. If patients expressed concerns, the nurse leader advocated for them so that the team could help resolve concerns.

> Nurse leaders have opportunities to use their knowledge and experience to bridge the gap between upper management and frontline care providers.

Successes and Lessons Learned

With every new initiative, it is important to reflect on the success and lessons learned during the process. Our first success was acceptance into the Early Experience Program. The demand for this new gene therapy was high, so the steering committee knew there was the potential that our application could be denied. Since Fox Chase administers a high volume of Bacillus Calmette-Guérin, gemcitabine, docetaxel, and mitomycin, this groundbreaking gene therapy needed to be explored for our patients. The application was submitted, several meetings were scheduled, and the application was accepted.

Cancer treatment is an emotional journey, and the nursing team focused on providing psychosocial support to this group of patients. Because their prior treatments had failed, patients were excited about the clinical trial data in hopes that a cystectomy could be avoided. Nurses supported patients as they expressed a full range of emotions from fear, worry, hope, and cautious optimism. Causal conversations with patients during treatment created a therapeutic bond that cannot be measured. Not only was implementation of this new gene therapy a success, but it also came with lessons learned; one important takeaway was that when patients are facing a life-altering decision with fear and sadness, a simple gesture can make a big impact on their psychosocial well-being.

Another key lesson learned is that any new process must be frequently reassessed to ensure the goal is being achieved. Frequent reassessment led to minor changes continually being made to our process. Communication was the most important tool in our arsenal. When communication started to break down, the nurse leader regrouped the team to reevaluate protocols.

Future Implications

True multidisciplinary health care teams offer unique perspectives to ensure that all aspects of a patient's condition are being addressed. When professionals with diverse expertise come together, they contribute different ideas and knowledge, which leads to more informed, well-rounded decisions. This collaborative approach reduces risk and oversight. Nurse leaders have opportunities to use their knowledge and experience to bridge the gap between upper management and frontline care providers. By doing so, these professionals help align the organizational or project management goals with patient-centered care, ensuring all strategies and decisions are practical and safe to implement in the clinical environment.

Including nurse leaders on multidisciplinary teams is fundamental because these leaders are patient advocates, care coordinators, quality experts, educators, and patient safety champions. A nurse leader's involvement enhances patient care because their presence contributes to more effective communication, improved patient outcomes, and a more cohesive team dynamic. OI

Rebecca Farrell MSN, RN, NEA-BC, is clinical manager at Fox Chase Cancer Center in Rockledge, Pennsylvania. Erin Longstreth-Papsun, MSN, RN, OCN, NEA-BC, is clinical director at American Oncologic Hospital: Fox Chase Cancer Center Network Operations in Philadelphia, Pennsylvania.

References

1. American Cancer Society. Key statistics for bladder cancer. Updated January 13, 2023. Accessed July 15, 2024. https://www.cancer.org/cancer/bladder-cancer/about/key-statistics.html

2. Holzbeierlein J, Bixler BR, Buckley DI, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline: 2024 amendment. *J Urol.* 2024; 211(4):533-538. doi:10.1097/JU.0000000000003846

3. ADSTILADRIN in patients with high grade, Bacillus Calmette-Guerin (BCG) unresponsive non-muscle invasive bladder cancer (NMIBC). Gov Identifier: NCT02773849. Last updated July 29, 2024. Accessed December 17, 20245. https://clinicaltrials.gov/ct2/show/NCT02773849

4. Boorjian SA, Alemozaffar M, Konety BR, et al. Intravesical nadofaragene firadenovec gene therapy for BCG-unresponsive non-muscle-invasive bladder cancer: a single-arm, open-label, repeat-dose clinical trial. *Lancet Oncol.* 2021;22:107-117. doi:10.1016/S1470-2045(20)30540-4