Nadofaragene firadenovec-vncg

An HCP Tool for AIM with Immunotherapy

Nadofaragene firadenovec-vncg (Adstiladrin) is indicated for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer with carcinoma in situ with or without papillary tumors. Guidelines from the National Comprehensive Cancer Network support using nadofaragene firadenovec-vncg in some patients with high-grade papillary Ta/T1 only tumors without carcinoma in situ.

Nadofaragene firadenovec-vncg is the first gene therapy for bladder cancer. It is also the first FDA-approved, non-replicating, adenoviral vector-based gene therapy for cancer. This drug is a suspension intended for intravesical instillation into the bladder.

Clinical trial results

In a Phase 3 CS-003 study, more than half of participants with carcinoma in situ ± Ta/T1 tumors, had a complete response within 3 months of a single dose of nadofaragene firadenovec-vncg. The response lasted for a median of 9.7 months, but ranged from 3 months to at least 52 months and was still going.

In a Phase 3, single-arm, multicenter, open-label, repeat-dose, study (NCT02773849), the following was observed:

- At 60 months, nearly half (49%) of the patients in the trial had bladder preservation (cystectomy-free).
- The overall survival at 60 months was 80% among patients with BCG-unresponsive non-muscle invasive bladder cancer. Among that group was 76% survival in patients with carcinoma in situ and 86% in patients with Ta/T1 cancer.

Pharmacology and Molecular Mechanism

Nadofaragene firadenovec-vncg (Adstiladrin) is a non-replicating gene therapeutic which introduces copies of the human interferon alpha-2b gene protein into urothelial cells of the bladder wall and tumor cells. After intravesical delivery and uptake of the gene, interferon alpha-2b will be transiently produced at the tumor site.

Subsequently, the protein made will elicit an immune response to have direct and indirect anti-tumor effects. The anti-tumor response induces apoptosis of bladder cancer cells and stifles angiogenesis to the tumor. Ultimately these effects should be cytotoxic, preventing the tumor from further growth and expansion.

DRUG DOSAGE AND ADMINISTRATION

Nadofaragene firadenovec-vncg is administered at a dose of 75 mL and concentration of 3 x 10^{11} viral particles (vp)/mL. The drug is instilled into the bladder via urinary catheter once every 3 months.

The drug comes frozen in a shipping container carton supplied as a suspension in 4, clear, single-use, glass vials. Each of the glass vials contains an extractable volume of not less than 20 mL. For administering nadofaragene firadenovec-vncg, all four vials comprise one dose for the patient. The suspension is not intended for topical, intravenous infusion or oral administration. It can be stored for 3 months in the freezer. In contrast to BCG, nadofaragene firadenovec-vncg does not require a biological safety cabinet for preparation. Nadofaragene firadenovec-vncg must be thawed and brought to room temperature before instillation, as cold fluid may precipitate urinary urgency and bladder spasm. Thawing may take several hours.

Premedication is recommended for patients before each instillation of nadofaragene firadenovec-vncg into the bladder. An anticholinergic is recommended to help prevent urinary voiding symptoms and retain the instillation for 1 hour in the bladder.

Once it is instilled into the bladder for treatment, it should remain there for 1 hour. Repositioning the patient is recommended every 15 minutes during the 1-hour instillation period to maximize surface area exposure on the bladder wall. After the 1-hour dwell time expires, the patient should void the therapeutic and completely empty the bladder. The voided urine should be disinfected with an equal volume of virucidal agent for 15 minutes prior to flushing toilet. Toilet should not be used by others during this disinfection time.

In clinical trials, nadofaragene firadenovec-vncg was used for an initial 12-month treatment period (four doses), and then it was used for subsequent optional treatment for up to 5 years. The “optional” treatment duration is up to the discretion of the treating physician. It may be used until unacceptable toxicity or recurrent high-grade non-muscle invasive bladder cancer.

SIDE EFFECTS AND MANAGEMENT

The most common (>10%) adverse reactions associated with nadofaragene firadenovec-vncg, including laboratory abnormalities (>15%), were bladder spasm, dysuria (painful urination), micturition (urinary urgency), hematuria (blood in urine), instillation site discharge, pyrexia (fever), chills, fatigue, and laboratory abnormalities (increased serum creatinine, glucose and triglycerides; decreased phosphate).

In the CS-003 clinical trial, approximately 33% of the participants had instillation site discharge. Another 24% reported fatigue and 20% reported bladder spasms, all of which were Grades 1 or 2. There were no Grade 3 or 4 reactions.

Laboratory abnormalities in clinical trials included an increase in glucose (38%), with 6% reporting Grade 3 or 4. Triglycerides were increased in 30% of participants overall, with 1.9% being Grade 3 or 4.

Warnings and Precautions

There are two warnings/precautions associated with nadofaragene firadenovec-vncg, including delaying treatment and viral dissemination. Additionally, for those female patients of reproductive potential, it is important to use effective contraception throughout treatment and then for 6 months following the last dose of nadofaragene firadenovec-vncg. No human clinical or animal reproductive and developmental toxicity studies have not been conducted with this agent. Use appropriate caution and assume a potential risk to a fetus.

Risk of Adenovirus Infection

Although there is a low risk for contact with adenovirus, health care staff should not be involved in the preparation or instillation of nadofaragene firadenovec-vncg if they are immunosuppressed or immune-deficient. Those in charge need to ensure appropriate communication, training, and accommodation for the health care team when preparing and dispensing this therapeutic.

This is also the case with other persons who are immunocompromised or immunosuppressed – they should not come into contact with nadofaragene firadenovec-vncg. There is a low-level shedding that may occur in urine. For 2 days following treatment, patients and caregivers need to be aware to disinfect urine for 15 minutes with an equal volume of bleach before flushing. This may equal half a cup of bleach.

Risk of Muscle Invasive or Metastatic Bladder Cancer with Delayed Cystectomy

Another warning with nadofaragene firadenovec-vncg is delaying cystectomy in patients. This could lead to the potentially lethal development of muscle invasive or metastatic bladder cancer. Therefore, if patients with carcinoma in situ do not have a complete response to treatment after 3 months or if the carcinoma in situ recurs, then cystectomy should be considered.

QUESTIONS & ANSWERS

Q. **How is nadofaragene firadenovec-vncg given?**

A. The drug is given as an intravesical delivery through a catheter, into the urethra and then into the bladder. There nadofaragene firadenovec-vncg stays for 1 hour so that the gene therapy has sufficient time to come into contact with bladder cells along the cell wall. After 1 hour, the agent is eliminated from the bladder by voiding.

Q. **Is there information about specific populations that should be known prior to using nadofaragene firadenovec-vncg?**

A. The agent is approved in adults and there is a lack of safety and effectiveness established for pediatric use. In the clinical studies, there were not sufficient numbers of patients under 65 years of age. Therefore, it cannot be determined whether the safety and efficacy of this agent differs between younger and older patients. No overall differences were observed between male and female patients.

Q. **What should patients tell their clinicians before receiving nadofaragene firadenovec-vncg?**

A. Patients should tell their doctors if they are taking other substances. This includes prescription medications, over-the-counter therapeutics, all vitamins, and any herbal supplements. Some of these may have unknown (to the patient or caregiver) affects on the drug's activity.

Q. **What adverse effects of nadofaragene firadenovec-vncg have been reported?**

A. The Phase 2 clinical trial (n=19 patients) demonstrated that nadofaragene firadenovec-vncg can cause some adverse effects. In the study, 100% of patients experienced at least one adverse event, with the highest severity being Grade 1 or 2 for most of the study's participants (n=16; 84.2%). Grade 3 events occurred in the other patients (15.8%), which were abdominal pain, dysuria, and acute renal failure (n=3). There were no Grade 4 or higher events reported in the Phase 2 trial.

In a Phase 3 trial (n=157), there were 58 patients that had dose interruptions. Again, most of these were mild Grade 1 or 2. Only 6 patients reported Grade 3 events. No Grade 4 or higher events were reported.

PATIENT RESOURCES

ADDITIONAL INFORMATION RESOURCES

American Cancer Society
Patient programs, services, 24/7 hotline, etc
https://www.cancer.org/

National Cancer Institute
Information about cancer types, treatment, side effects, find a clinical trial, etc
https://www.cancer.gov/

FINANCIAL ASSISTANCE

Cancer Financial Aid Coalition
Facilitates communication, educates and advocates for patients.
www.cancerfac.org

Centers for Medicare and Medicaid Services (CMS)
Apply to determine if you are eligible for government assistance.
www.cms.gov or www.medicare.gov
800-633-4227

Lazarex Foundation
Provides assistance with travel costs for clinical trial participation. Ask your social work counselor for a referral if you have been consented to a clinical trial for melanoma.
www.lazarex.org

Needymeds
Database to search for free or low-cost medications, help with medical transportation and other resources.
www.needymeds.org

Patient Advocate Foundation
Provides assistance with mediation, financial stability, and other assistance. Funds subject to availability.
Patient must meet their eligibility for financial assistance.
www.patientadvocate.or
g 800-532-5274

Expect Miracles Foundation
The Sam Fund for Young Adult Survivors of Cancer assists ages 21-39 with their transition into post-treatment life. This program distributes grants and scholarships in an effort to enable survivors to pursue goals.
www.thesamfund.org
info@thesamfund.org

PRESCRIPTION ASSISTANCE

CancerCare Co-Payment Assistance Foundation
Helps with the cost of medication. Availability of funds for patients with specific cancers is subject to availability.
www.cancercarecopay.org
1-866-552-6729

Medicine Assistance Tool
Database to search for patient assistance resources offered by pharmaceutical companies.
www.medicineassistancetool.org/

Patient Advocate Foundation Co-Pay Relief
Provides direct financial support to patients who medically qualify. Funds subject to availability.
https://copays.org
1-866-512-3861

Good Days
Provides assistance with insurance co-pays, and prescription medications. Funds subject to availability.
www.mygooddays.org

Health Well Foundation
For patients who cannot afford insurance premiums, co-payments, co-insurance, or other out-of-pocket health care costs. Funds for patients subject to availability. Patient must also meet eligibility for financial assistance.
www.healthwellfoundation.org or grants@healthwellfoundation.org
1-800-675-8416

The Assistance Fund, Inc
Provides prescription copay and financial assistance, including health insurance premiums. Funds subject to availability.
www.theassistancefund.org
https://tafcares.org
1-855-845-3663

PAN Foundation
Provides financial assistance to cover out-of-pocket treatment costs. Funds subject to availability.
www.panfoundation.org
1-866-316-PANF (7263)

Patient Assistance Program
Comprehensive database of patient assistance programs offering free medications.
www.rxassist.org
info@rxassist.org

HOUSING

American Cancer Society – Hope Lodge
Provides free housing during treatment appointments. Requires a referral from your social worker.
www.cancer.org/
1-800-227-6333.

American Cancer Society – Extended Stay America
Partnership to offer discounted rooms for patients who have to be away from home for cancer treatment.
https://www.cancer.org/about-us/our-partners/extended-stay-america.html
1-800-227-2345

Healthcare Hospitality Network
Connects patients and their caregivers looking for lodging near their healthcare provider
https://members.hhnetwork.org/locate-a-house
1-800-318-8861

Joe's House
Helping patients with cancer find lodging throughout the U.S.
https://www.joeshouse.org/lodging?state=0
1-877-563-7468

National Council of State Housing Agencies
Emergency rental assistance programs available by state. Federal grants still available in some areas.
https://www.ncsha.org/emergency-housing-assistance/

TRANSPORTATION (AIR AND GROUND)

Air Charity Network
Provides access for people in need who are seeking free air transportation to specialized health care facilities
http://aircharitynetwork.org/
1-877-621-7177

Corporate Angel Network
Nonprofit organization that helps cancer patients by arranging free travel on corporate aircraft
https://www.corpangelnetwork.org/
info@corpangelnetwork.org
1-914-328-1313

Medicaid
Ground transportation only. Sets up rides and provides mileage reimbursement for Medicaid patients only.
1-877-633-8747

Mercy Medical Angels
Provides free medical transportation (flights, gas cards, bus and train tickets) for patients with financial needs who need to travel more than 50 miles. Patients must meet their eligibility for financial assistance.
www.mercymedical.org/

Pilots for Patients
Provides free flights to people in need of medical treatment. Patient must be medically stable to fly and be ambulatory. Ask your social worker about a referral.
www.pilotsforpatients.org
318-322-5112

ADDITIONAL RESOURCES

ADSTILADRIN (nadofaragene firadenovec-vncg) suspension, for intravesical use [prescribing information]. Kastrup, Denmark and Kuopio, Finland: Ferring Pharmaceuticals. Available at: https://ferringusa.com/wp-content/uploads/sites/12/2024/10/Adstiladrin_PI.pdf. Updated August 2024. Accessed May 2025.

Colbert L, Jia Y, Sharma A et al. FDA Approval Summary: Nadofaragene Firadenovec-vncg for Bacillus Calmette-Guérin-Unresponsive Non-Muscle-Invasive Bladder Cancer. *Clin Cancer Res*. 2025;31(7):1182-1185. doi: 10.1158/1078-0432.CCR-24-2812.

Holler SD and Smith SM. Practical use of nadofaragene firadenovec-vncg for pharmacists. *J Oncol Pharm Pract*. 2025;31(3):488-494. doi: 10.1177/10781552251315146.

Konety BR, Lotan Y, and Myers A. Safety of nadofaragene firadenovec-vncg: review of data from phase 2 and phase 3 studies. *Can J Urol*. 2025;32(1):29-36. doi: 10.32604/cju.2025.064710.

Narayan VM, Boorjian SA, Alemozaffar M et al. Efficacy of Intravesical Nadofaragene Firadenovec for Patients With Bacillus Calmette-Guérin-Unresponsive Nonmuscle-Invasive Bladder Cancer: 5-Year Follow-Up From a Phase 3 Trial. *J Urol*. 2024;212(1):74-86. doi: 10.1097/JU.0000000000004020.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Bladder Cancer. Version 4.2024 Plymouth Meeting, PA: National Comprehensive Cancer Network; 2024.