## BACKGROUND

**Nadofaragene firadenovec** is a novel intravesical gene therapy (FDA approved in Dec 2022) for treatment of Bacillus Calmette–Guérin (BCG)-unresponsive, high-risk non-muscle invasive bladder cancer (NMIBC)[1]

**Pembrolizumab** is an intravenous humanized antibody (approved in January 2020) for treatment of BCG-unresponsive NMIBC patients with carcinoma in-situ (CIS)[2]

Drug price for nadofaragene firadenovec is not yet known. There is **limited evidence on cost-effectiveness** of treatments for high-risk NMIBC patients for whom prior immunotherapy or chemotherapy was ineffective

Given the **paucity of treatment alternatives** and small sample sizes in interventional and observational studies, there is considerable uncertainty around published estimates of NMIBC recurrence and progression

## METHODS

- A **cohort simulation Markov model** was developed with health states for initial treatment, recurrent/persistent NMIBC, MIBC, metastatic disease, post-cystectomy and death. Model inputs were obtained from clinical trial data and systematic literatures reviews.

**Populations**: BCG-unresponsive NMIBC patients with carcinoma in-situ (CIS) ± Ta/T1 disease, and those with Ta/T1 only (non-CIS)

**Interventions**: Nadofaragene firadenovec and pembrolizumab

**Comparators**: Hypothetical treatments for CIS ± Ta/T1, and for Ta/T1 only (non-CIS)

**Outcomes**: Total costs, total QALYs, incremental cost-effectiveness ratio (ICER), individual and population EVPI and EVPPI

**Model specifications**: Lifetime horizon, 3-month cycle length, 3% annual discount rate for costs and QALYs

**Perspective**: United States health system (only direct medical costs included

**Willingness to pay threshold (WTP)**: $150,000 per QALY gained

- A **placeholder annual price** for nadofaragene firadenovec, 10% greater than that of pembrolizumab, was used
- In **probabilistic sensitivity analysis** (PSA), model inputs were varied simultaneously for 10,000 iterations using beta distributions for probability and utility inputs, and gamma distributions for cost inputs
- Value of information analysis was conducted using a **single-loop Monte-Carlo scheme**[3]
- EVPPI was obtained by varying only the **deterministically most influential model input** (probability of disease progression from NMIBC to MIBC)
- Based on the estimated incidence of bladder cancer in 2022[4], and assuming that 70% cases were of NMIBC[5], of which 40% were unresponsive to BCG therapy[6], a **constant annual incidence rate** of 22,730 new BCG-unresponsive NMIBC cases was used for obtaining population EVPI

References: [1]Adstiladrin [package insert]. Ferring Pharmaceuticals BV, Denmark. 2022. Available at: https://www.fda.gov/media/164029/download. Accessed: 23rd April, 2023. [2]Keytruda [package insert]. Merck & Co., Inc., USA. 2014. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125514s096lbl.pdf. Accessed: 23rd April, 2023. [3]K.M. Wymer, V. Sharma, C.S. Saigal, et al. Cost-effectiveness analysis of pembrolizumab for bacillus Calmette-Guérin-unresponsive carcinoma in situ of the bladder. J Urol, 205 (5) (2021), pp. 1326-1335. [4]Cancer Stat Facts: Bladder Cancer. National Cancer Institute, Surveillance, Epidemiology, and End Results Program. https://seer.cancer.gov/statfacts/html/urinb.html. Accessed February 20, 2022. Z. [5]Kirkali, T. Chan, M. Manoharan, et al. Bladder cancer: epidemiology, staging and grading, and diagnosis. Urology, 66 (6 suppl 1) (2005), pp. 4-34. A.R. [6]Zlotta, N.E. Fleshner, M.A. Jewett. The management of BCG failure in non-muscle-invasive bladder cancer: an update Can Urol Assoc J, 3 (6 suppl 4) (2009), pp. S199-S205

# Cost-Utility and Value of Information Analysis of Novel Treatments for BCG-Unresponsive Non-Muscle Invasive Bladder Cancer

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## OBJECTIVES

**1. To model the lifetime costs, QALYs and incremental cost-effectiveness ratio for nadofaragene firadenovec and pembrolizumab, compared to hypothetical treatment comparators based on approved and investigational therapies**
**2. To estimate the individual and population expected value of perfect information (EVPI) and expected value of partial perfect information (EVPPI) for nadofaragene firadenovec and pembrolizumab**

## CONCLUSIONS

**Cost-effectiveness of nadofaragene firadenovec will depend upon its price. A 5.4% reduction in the current price of pembrolizumab will make it cost-effective in the CIS population.**

**The value of eliminating uncertainty around estimates for NMIBC progression was close to the value of obtaining perfect information, suggesting that further research on disease progression would be valuable to decision makers.**

**BCG-unresponsive NMIBC has a substantial impact on quality of life and direct medical costs. The value of obtaining cost-effectiveness model inputs with greater certainty is considerable, especially for treatments with an ICER close to the WTP threshold.**

Scan to access the full paper on this cost-effectiveness analysis.

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## RESULTS

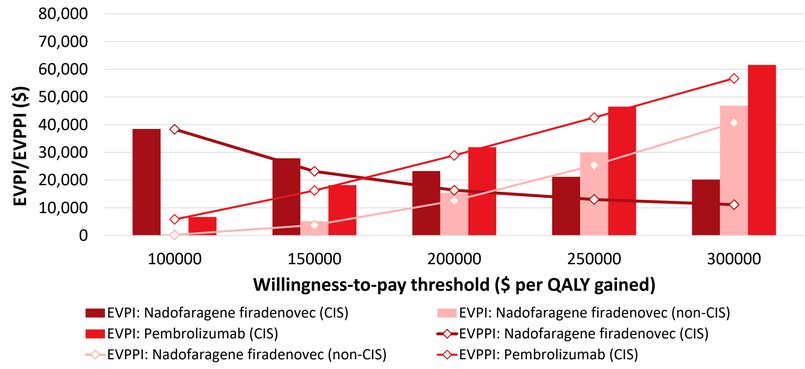
**I. Base-case results: Total costs in 2021 US dollars, total quality-adjusted life years (QALYs) and incremental cost-effectiveness ratio (ICER) for each treatment and comparator arm**

| Treatment | Total costs | Total QALYs | ICER ($ per QALY gained) |
|---|---|---|---|
| **CIS population** | | | |
| Nadofaragene firadenovec | $346,101 | 5.15 | **263,233** |
| Pembrolizumab | $286,042 | 5.02 | **167,677** |
| Comparator | $240,297 | 4.75 | |
| **Non-CIS population** | | | |
| Nadofaragene firadenovec | $340,221 | 5.51 | **145,394** |
| Comparator | $239,416 | 4.81 | |

**II. PSA results: Proportion of iterations in which the treatment was cost-effective, for a range of WTP thresholds**

| Treatment | Willingness to pay threshold ($ per QALY gained) | | | | |
|---|---|---|---|---|---|
| | 100,000 | 150,000 | 200,000 | 250,000 | 300,000 |
| **CIS population** | | | | | |
| Nadofaragene firadenovec | 3.04% | 17.44% | 34.38% | 48.06% | 57.71% |
| Pembrolizumab | 30.23% | 48.82% | 58.79% | 64.87% | 68.58% |
| **Non-CIS population** | | | | | |
| Nadofaragene firadenovec | 32.64% | 55.59% | 67.38% | 74.60% | 78.64% |

**III. Individual EVPI and EVPPI in 2021 US dollars, for a range of WTP thresholds**




**IV. Population EVPI in 2021 US dollars at a $150,000 WTP threshold**