Intravesical Gemcitabine/Docetaxel (Gem/Doce) Fact Sheet

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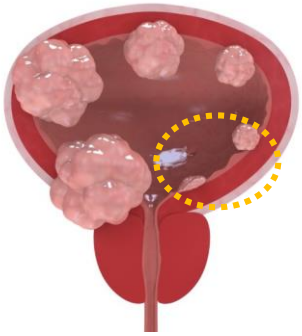


Non-Muscle Invasive Bladder Cancer (NMIBC)

What constitutes Gem/Doce therapy?

Sequential ***intravesical*** gemcitabine and docetaxel (Gem/Doce) therapy consists of two drugs, Gem and Doce, used in sequence one right after the other. It was first described by Dr. Michael O'Donnell and colleagues in 2015 at the University of Iowa in the US for NMIBC patients in whom BCG therapy had failed ***[1].***

Indications for Gem/Doce

Intravesical Gem/Doce therapy may be used for intermediate and high-risk BCG-unresponsive NMIBC patients who are unfit or refuse surgery for bladder preservation ***[2–6].*** It has also been shown to work at least as well as BCG for first-line therapy of intermediate and high-risk BCG-naïve NMIBC, mainly when BCG therapy is unavailable ***[7-10].***

Cancer efficacy of Gem/Doce

Weighted mean RFS		**BCG states**
12 months	24 months	
60%	42%	BCG failure
80%	75%	BCG naïve

Weighted mean PFS	**BCG status**
92%	BCG failure
98%	BCG naïve

Long term follow-up (5 years) Oncological outcomes	
Progression-free survival	82%
Cystectomy-free survival	75%
Cancer-specific survival	91%
Overall survival	64%

Cystectomy rate BCG failure	**Treatment**
10-35%	Gem/Doce
3-50%	BCG

RFS: Recurrence-Free Survival
HG RFS: High-Grade RFS
PFS: Progression-Free Survival

Gem/Doce Protocol

Sequential administration of ***1g Gem*** in 50ml NS (60-90 min), then drain and give ***Doce 37.5 mg*** in 50 cc NS (60–90 min).

Pre-treatment Recommendations:

-Avoid/restrict excess fluid, caffeine, alcohol, and diuretics 4-6 hours prior.

-Oral sodium bicarbonate (1300 mg) night before and morning of Gem/Doce to reduce urine acidity from Gem.

-Oral ondansetron (4 mg) and/or naproxen (220-250 mg)/ ibuprofen (600 mg) if nausea or bladder pain occur, respectively.

-Antispasmodics for patients with bladder irritability or spasms.

Cost of therapy

-The mean costs per patient at 2 years is approximately $12,363 for BCG therapy vs. $7,090 for Gem/Doce ***[11].***

- Radical Cystectomy costs at 90 days is more than $50,000.

-4-7% of recurrences are limited to Ta low grade (LG). Accordingly, the HG RFS is ≈ 4-7% higher than the overall RFS.

Efficacy of Gem/Doce vs. BCG therapy in BCG naïve patients

Weighted mean RFS		Therapy
12 months	24 months	
70%	60%	BCG
80%	75%	Gem/Doce

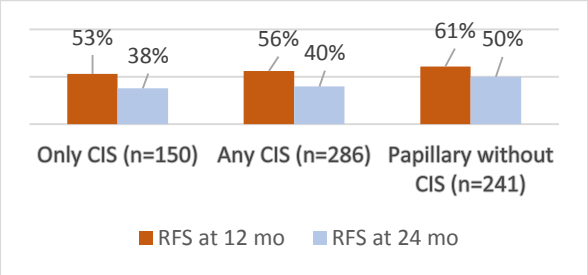
High-risk NMIBC

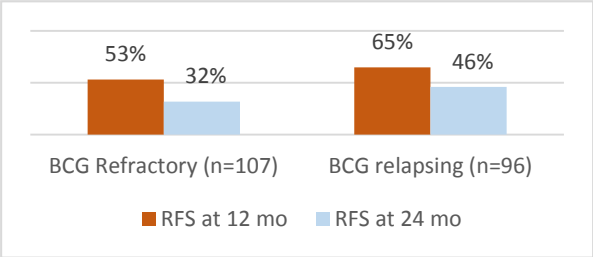
Weighted mean RFS		Therapy
12 months	24 months	
82%	74%	BCG
84%	76%	Gem/Doce

Intermediate-risk NMIBC

Gem/Doce has shown **better efficacy** than BCG for high-risk disease and **similar efficacy** for intermediate-risk disease. These results are based on cohort studies.

Gem/Doce results for BCG failures





Average results from multiple published clinical trials

BCG failures

Gem/Doce generally **works better** for high-grade papillary tumors without CIS and in BCG relapsing vs. refractory cases (recurrence after achieving a disease-free state at 6 months after adequate BCG vs. never disease free after BCG).

For BCG-failure intermediate risk disease, all tumor stages and grades appear to be **equally responsive** to Gem/Doce.

Patients with high-risk disease who fail on BCG therapy will benefit from a **monthly maintenance** regimen of Gem/Doce **for 24 months.** This is associated with better 2-year RFS than patients who did not receive maintenance therapy. Hazard ratio = 2.37

Toxicity of Gem/Doce therapy

- Documented toxicity of Gem/Doce is generally ***mild*** in most studies. ~50% report no side effects.
- Grade III or higher adverse events are ***rare <1%.***
- Most adverse events are related to ***irritative urinary symptoms*** *(dysuria, frequency, hematuria).* However, ***mild-moderate tiredness*** lasting 1-2 days and/or ***mild nausea*** < 24 hours may also occur.
- Adverse events that affect treatment schedules range from **6% to 16%.**
- Only about **3-4%** of patients are unable to tolerate a full 6 weeks' induction regimen (vs. **10%** for BCG).

-Local side effects from BCG therapy occur in ~**60%** of cases, and systematic side effects occur in up to **35%** of cases. Overall **5%** are serious.

-Treatment regimens are affected by BCG toxicity (delay or discontinuation) in up to **30%** of cases.

Future directions

A Randomized Phase III Trial of **Intravesical BCG** versus **Intravesical Docetaxel and Gemcitabine** Treatment in BCG Naive Non-Muscle Invasive Bladder Cancer **(The BRIDGE Trial)**

Status: recruiting

Supporting Medical Literature

1-Steinberg RL, Thomas LJ, O'Donnell MA, et al. Sequential Intravesical Gemcitabine and Docetaxel for the Salvage Treatment of Non-Muscle Invasive Bladder Cancer. Bladder Cancer. 2015;1(1):65-72.

2-Chevuru PT, McElree IM, Mott SL, et al. Long-term follow-up of sequential intravesical gemcitabine and docetaxel salvage therapy for non-muscle invasive bladder cancer. Urol Oncol. 2023;41(3):148.e1-148.e7.

3-Steinberg RL, Thomas LJ, Brooks N, et al. Multi-Institution Evaluation of Sequential Gemcitabine and Docetaxel as Rescue Therapy for Nonmuscle Invasive Bladder Cancer. J Urol. 2020;203(5):902-909.

4-Steinberg RL, Packiam VT, Thomas LJ, et al. Intravesical sequential gemcitabine and docetaxel versus bacillus calmette-guerin (BCG) plus interferon in patients with recurrent non-muscle invasive bladder cancer following a single induction course of BCG. Urol Oncol. 2022;40(1):9.e1-9.e7.

5-Milbar N, Kates M, Chappidi MR, et al. Oncological Outcomes of Sequential Intravesical Gemcitabine and Docetaxel in Patients with Non-Muscle Invasive Bladder Cancer. *Bladder Cancer*. 2017;3(4):293-303.

6- Yim K, Melnick K, Mott SL, et al. Sequential intravesical gemcitabine/docetaxel provides a durable remission in recurrent high-risk NMIBC following BCG therapy [published online ahead of print, 2023 Sep 8]. Urol Oncol. 2023;S1078-1439(23)00229-6.

7-McElree IM, Steinberg RL, Martin AC, et al. Sequential Intravesical Gemcitabine and Docetaxel for bacillus Calmette-Guérin-Naïve High-Risk Nonmuscle-Invasive Bladder Cancer. J Urol. 2022;208(3):589-599.

8-McElree IM, Steinberg RL, Mott SL, et al. Comparison of Sequential Intravesical Gemcitabine and Docetaxel vs Bacillus Calmette-Guérin for the Treatment of Patients with High-Risk Non-Muscle-Invasive Bladder Cancer. JAMA Netw Open. 2023;6(2):e230849.

9-Babajide R, Labbate C, Saoud R, et al. Early Experience with Intravesical Gemcitabine-Docetaxel for BCG-Naïve Patients with High Grade Non-Muscle Invasive Bladder Cancer. Urol Oncol 2020;38:901.

10-Tan WS, McElree IM, Davaro F, et al. Sequential Intravesical Gemcitabine and Docetaxel is an Alternative to Bacillus Calmette-Guérin for the Treatment of Intermediate-risk Non-muscle-invasive Bladder Cancer. Eur Urol Oncol. 2023 Oct;6(5):531-534. doi: 10.1016/j.euo.2023.06.011. Epub 2023 Jul 18. PMID: 37468392.

11-Bukavina L, Bell S, Packiam VT, et al. Sequential intravesical gemcitabine-docetaxel vs. bacillus Calmette-Guerin (BCG) in the treatment of non-muscle invasive bladder cancer: A preliminary cost-effectiveness analysis. *Urol Oncol*. 2023;41(9):391.e1-391.e4.