Intravesical Valrubicin/Docetaxel (Val/Doce) Fact Sheet

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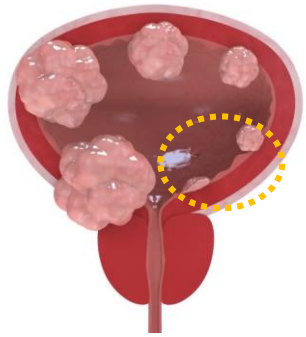

Non-Muscle Invasive Bladder Cancer (NMIBC)

What constitutes Val/Doce therapy?

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

Val/Doce Protocol

Administration of ***800 mg Val*** in 75 ml NS **(90 min)**, then drain and give ***Doce 37.5 mg*** in 50 cc NS **(90-120 min).**

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

-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.

Indications for Val/Doce therapy

Intravesical Val/Doce therapy may be used for high-risk recurrent NMIBC patients following the failure of BCG and/or Gem/Doce therapy. These patients are usually unfit or refuse radical cystectomy ***[1].*** When Val/Doce is used as salvage therapy, a large percentage of patients are able to keep their bladders at an acceptable rate of progression, avoiding death from bladder cancer ***[1].***

Important note for Val instillation

Because Val frequently results in **immediate** pain and bladder irritation, **alkalinized lidocaine** (**40 cc of 2% lidocaine** mixed with **4 cc of standard sodium bicarbonate 8.4%** liquid) is given to all patients intravesically for **10–15 minutes** prior to Val instillation to avoid pain and bladder spasm.

Cancer Efficacy of Val/Doce

RFS		Disease grade
12 months	24 months	
82%	73%	Low-grade
56%	38%	High grade

OS	Disease grade
90%	Low-grade
87%	High-grade

PFS and cystectomy rate among high-grade disease at 24 months	
Progression-free survival	82%
Cystectomy rate	14%

Survival outcomes at 24 months	Treatment
CSS	96%
CFS	84%

RFS: Recurrence-Free Survival
CSS: cancer-specific survival
CFS: cancer-free survival
PFS: progression-free survival
OS: overall survival

Median follow-up time ~24 months

Induction and maintenance therapy

Induction regimen: once weekly for **six weeks.**
Maintenance regimen: monthly therapy for 24 months that replicates the same dose as induction should be given if disease-free at the first follow-up.

Prior intravesical therapy

Prior intravesical therapy (%)	
Gem/Doce	93%
BCG	72%
Both Gem/Doce and BCG	68%
Other intravesical therapy	33%

Val/Doce has been assessed in **pre-treated NMIBC** patients (who received previous intravesical therapy but failed that therapy).

In the trial assessing efficacy of **Val/Doce**: there were 42 patients (**67% of the high grade (HG)** group) with **CIS containing disease** immediately prior to Val/Doce induction and 58 patients (**87% of the HG group**) with **any history of CIS. Total n=75.** ***[1]***

Previously, in a phase II/III open-label study, **single-agent valrubicin** showed a **complete response rate of only 18%** in patients **with CIS** after BCG failure vs. **60% with Val/Doce** ***[1, 2].***

Furthermore, Val/Doce was **equally effective** regardless of when Gem/Doce failed, either immediately or during maintenance therapy.

Toxicity of Val/Doce therapy

	Grade 1	Grade 2
Total reported adverse events (%)	54%	46%
Specific events (%)		
Dysuria	11%	3.7%
Hematuria	9.3%	3.7%
Urinary frequency/urgency	15%	3.7%
Bladder spasm	-	33%
Nausea	7.4%	-
Fatigue	9.3%	-
Arthralgia	1.9%	-
Shortness of breath	-	1.9%

Val/Doce was well tolerated, with **only 2 (2.7%)** patients unable to receive a full induction.

Roughly half of the patients were having only minor side effects ***[1].***

Intravesical **valrubicin, systemic pembrolizumab, nadofaragene firadenovec (Adstiladrin**; adenoviral vector-based gene therapy), and **nogapendekin alfa inbakicept-pmln (Anktiva)** are the only FDA-approved treatments for recurrent BCG-unresponsive CIS with 1-year complete response rates of 14%, 19%, 24% and 36%, respectively. *[3,4].*

JUST THE FACTS

- In a systematic review of 160 real-world studies, **<20% of patients** with recurrent high-risk NMIBC after BCG therapy underwent RC ***[5].***
- In a survey in the US evaluating the practice pattern of urologists (n=259) in treating BCG-unresponsive disease, **only 24% of urologists** routinely performed **RC** for those patients ***[6].***
- In a recent multi-country survey, **89% of patients with BCG unresponsive** disease never chose **RC** as their preferred option in the choice experiment ***[7].***

-**Radical cystectomy (RC)** remains the gold standard therapy for BCG unresponsive disease, according to different urology guidelines, however:

-RC has a significant complication rate **(59%-64%)**, with **13%-15%** requiring surgical intervention ***[8-9]***

- Many patients with BCG unresponsive disease ***are unfit for RC or refuse to undergo this procedure***. There are no guidelines that help in managing these patients.

Considering the high 2-year CSS of 96%, bladder-sparing treatment can be offered to appropriately selected patients who have **BCG and/or Gem/Doce unresponsive disease**.

Supporting Medical Literature

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2- Dinney CP, Greenberg RE, Steinberg GD. Intravesical valrubicin in patients with bladder carcinoma in situ and contraindication to or failure after bacillus Calmette-Guérin. Urol Oncol. 2013;31(8):1635-1642.

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4-https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nogapendekin-alfa-inbakicept-pmln-bcg-unresponsive-non-muscle-invasive-bladder-cancer.

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6-Abou Chakra M, Shore ND, Dillon R, O'Donnell MA. US Clinical Practice Patterns of Intravesical Chemotherapy for Bacillus Calmette-Guérin-Unresponsive and Bacillus Calmette-Guérin-Exposed Nonmuscle-Invasive Bladder Cancer. Urol Pract. 2024;11(1):97-107.

7-Collacott H, Krucien N, Heidenreich S, Catto JWF, Ghatnekar O. Patient Preferences for Treatment of Bacillus Calmette-Guérin-unresponsive Non-muscle-invasive Bladder Cancer: A Cross-country Choice Experiment. Eur Urol Open Sci. 2023;49:92-99.

8-Novara G, Catto JW, Wilson T, et al. Systematic review and cumulative analysis of perioperative outcomes and complications after robot-assisted radical cystectomy. Eur Urol. 2015;67(3):376-401.

9-Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. Eur Urol. 2009;55(1):164-174.