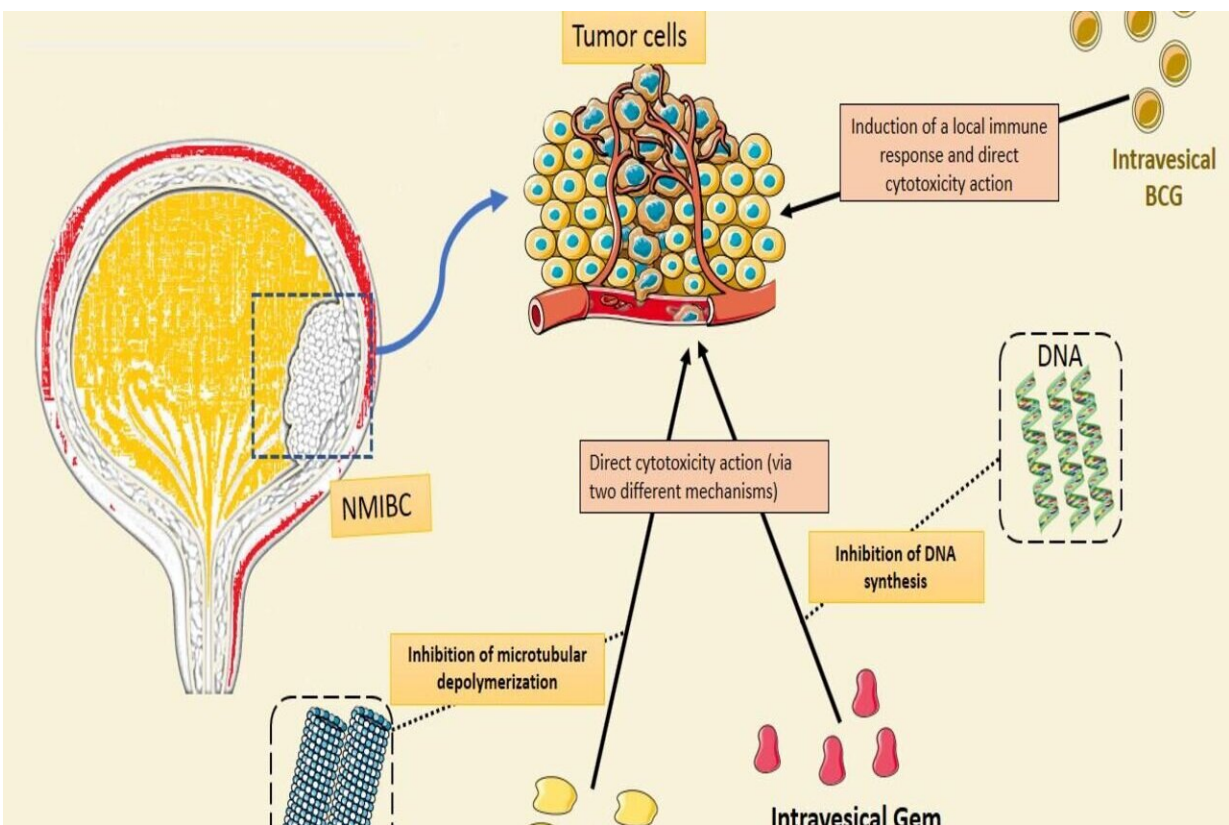


Intravesical gemcitabine/docetaxel as an alternative therapy for patients with non-muscle-invasive bladder cancer

February 23 2024, by Michael A. O'Donnell and Mohamad Abou Chakra



NMIBC: non-muscle invasive bladder cancer; BCG: Bacillus Calmette-Guérin; Gem: gemcitabine; Doce: docetaxel. Parts of the figure were drawn using Servier Medical Art, licensed under a Creative Commons Attribution 3.0 Unported License (<https://creativecommons.org/licenses/by/3.0/>).

Bladder cancer is one of the more common cancers worldwide. It is considered a major health care problem with a high financial burden. Of these cases, 75% are non-muscle-invasive, which characterizes dangerous diseases with a high risk of recurrence (up to 70% within five years of diagnosis) and progression (up to 40% within five years of diagnosis).

Treatment relies on a risk stratification strategy where risk groups are identified based on tumor characteristics and recurrence history: low risk, intermediate risk and high risk.

The [treatment guidelines](#) for non-muscle-invasive bladder cancer (NMIBC) consist of endoscopic resection of the tumor, then administration of drugs into the bladder (intravesical therapy), typically with weekly instillation for six weeks (induction therapy) followed by additional instillations (maintenance therapy) every three or six months or monthly for one to three years.

Intravesical bacillus Calmette-Guerin (tuberculosis vaccine) has been used as [adjuvant therapy](#) by urologists since 1976. Because of its reliable reduction in both recurrence and progression, it has become the standard of care for the treatment of HR NMIBC.

Unfortunately, despite its good clinical activity, BCG fails approximately 40% of patients in two years, leading to an ever-present need to develop rescue agents to avoid the need for bladder removal (cystectomy).

Since 2012, when contamination occurred at one of the two major suppliers of BCG resulting in its permanent closure, BCG has been in a worldwide shortage situation. While multiple trials were launched to investigate the use of alternative therapies such as intravesical chemotherapy, immunotherapy and gene therapy, both as a substitute for BCG as well as rescue treatment after BCG failure, none provided the

same level of efficacy, safety and affordability of BCG, until recently.

One of the most promising new strategies for NMIBC is the combination of intravesical chemotherapy drugs used as sequential therapy, one drug after the other, with one-hour bladder dwell time for each drug. Initial results with gemcitabine (Gem) and mitomycin C (MMC) appeared promising but shortages in MMC led to the need to substitute docetaxel (Doce) for MMC to create Gem/Doce.

Both were developed by Dr. Michael O'Donnell, professor and director of urologic oncology, at the University of Iowa (UI) in the U.S. Results for Gem/Doce were first reported in 2015 and since then it has been reported in more than 500 patients by multiple institutions.

To summarize the recent data accumulating on combination intravesical sequential chemotherapy for NMIBC, we performed a [systematic review](#) that has been published in *Expert Opinion on Pharmacotherapy*. We included data from 15 trials that were relevant to our aim that included data on Gem/MMC or Gem/Doce.

However, while reports of Gem/MMC were limited to failed BCG patients, with the evolving BCG shortage, Gem/Doce found a use for not only failed BCG patients but as a substitute for patients never previously receiving BCG (BCG naïve).

Efficacy in terms of cancer recurrence was expressed in terms of 24-month, recurrence-free survival. In the BCG-naïve group, the 24mRFS for Gem/Doce was ~77% for both HR (all high-grade) and IR (almost all low-grade) diseases. In the HR NMIBC BCG-failure setting, the overall 24mRFS for Gem/Doce was 42%.

Interestingly, Gem/MMC performed similarly well for BCG failures. In terms of side effects, the documented toxicity of Gem/Doce was found

to be generally mild in most studies with roughly half of patients reporting no side effects. Grade III (serious) or higher adverse events were rare (

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