# Introduction

Bladder cancer is recognized as one of the most prevalent malignancies worldwide, with approximately 20% of those diagnosed ultimately succumbing to the disease (**Warrick, Joshua I., et al. 2024**).

Bladder cancer exhibits the highest incidence in Europe, followed by the United States and Egypt **(Babjuk, Marko, et al. 2022).**

Bladder cancer is 3 to 4 times more common in men than women. It's incidence increase in the sixth decade of life **(Aveta, Achille, et al. 2022).**

It is the 2nd common site of cancer in men as it represent 12.7% **(Ibrahim, Nurul Khalida, et al. 2022).**

Transitional cell carcinoma (TCC) is the most common type of bladder tumor, presenting as a superficial disease at the time of initial diagnosis in approximately 75% of cases **(Gravas, Stavros, et al. 2023).**

Transurethral resection of bladder tumor(s) (TURBT), is considered the treatment of choice **(Mohanty, Sambit K., et al. 2023).**

Despite achieving visually complete resection, bladder cancer is associated with a high recurrence rate, potentially due to tumor cell implantation following transurethral resection of bladder tumor (TURBT) or the presence of residual microscopic disease. **(Zhang, Yongzhen, et al., 2018).**

The high rates of recurrence and stage progression present a significant clinical challenge. Intravesical instillation of chemotherapeutic or immunotherapeutic agents following transurethral resection of bladder tumor (TURBT) plays a crucial role in reducing the risk of recurrence and disease progression. Immunotherapeutic agents, such as Bacillus Calmette-Guérin (BCG), may enhance the body's immune response, exerting a direct effect on tumor cells **(Bazargan, Sarah, et al. 2023).**

Local side effects are observed in approximately 90% of patients receiving Bacillus Calmette-Guérin (BCG) therapy. More serious systemic complications may occur, including hemodynamic instability, persistent high-grade fever, allergic reactions such as arthralgia and rash, or involvement of solid organs (e.g., epididymitis, liver, lung, kidney, osteomyelitis, and prostate). These complications can necessitate discontinuation of treatment and, in some cases, have resulted in fatal outcomes **(Babjuk, Marko, et al. 2022).**

Despite the significant morbidity associated with BCG therapy, an improvement in overall survival has not been demonstrated, with only approximately two-thirds of patients showing a response to the treatment **(Claps, Francesco, et al. 2023).**

Research has thus focused on developing new drugs or novel drug combinations for intravesical instillation. Gemcitabine (GEM) has demonstrated efficacy with minimal bladder irritation and is generally characterized by rapidly self-resolving side effects **(Tomko, Andrea M. et al. 2022).**

Gemcitabine is an active systemic chemotherapeutic agent in the management of advanced bladder cancer and it has also been evaluated in the management of superficial disease **(Bazargan, Sarah, et al. 2023).**

Gemcitabine has a molecular weight of 299 Da, which is lower than that of most commonly used intravesical chemotherapeutic agents. This molecular size facilitates its penetration into the bladder mucosa, enhancing its therapeutic efficacy, while remaining sufficiently large to prevent significant systemic absorption. Additionally, its favorable pharmacokinetic profile makes gemcitabine an optimal candidate for regional therapy **(Li, Changjiu, et al. 2024).**

Intravesical gemcitabine is a promising drug that may be an option in treating patients with non muscle invasive bladder cancer **(Chen, Wujun, et al. 2022).**

Comparative trials of intravesical gemcitabine and Bacillus Calmette-Guérin (BCG) have yielded comparable outcomes regarding recurrence rates and disease progression, with the gemcitabine group experiencing fewer side effects **(Bazargan, Sarah, et al. 2023).**

# Aim of The Work

The aim of this work is to evaluate the efficacy and

safety of Gemcetabine as a local intravesical adjuvant

treatment of non muscle invasive TCC in reducing the risk

of recurrence and progression after TURBT in comparison

to BCG.

# Chapter (1) Non Muscle Invasive Bladder Cancer

**Introduction and incidence**

Bladder tumor is the 9th most commonly diagnosed tumor in the world and the 2nd most common malignancy of the urogenital tract **(Chen, Ji-Qing, et al. 2022).** It's causing more than 130,000 deaths annually **(ŞEN, Selda, et al. 2021).**