E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/15.01.217

Research Article

Advancements in Immunotherapeutic and Targeted Approaches for Bladder Cancer Treatment

Muhammad Ameen[1], Urooj Niazi[2], Saadat Hassan Hashmi[3], Yassar Hussain Patujo[4], Ahmed Sajjad[5], Ghulam Mujtaba[6]

[1]Senior Registrar Urology, Benazir Bhutto Hospital / Rawalpindi Medical University (RMU) Rawalpindi Pakistan.

[2]House officer, Pakistan Institute of Medical Sciences Islamabad Pakistan.

[3]Chief Consultant Urologist, Benazir Bhutto Hospital / Rawalpindi Medical University (RMU) Rawalpindi Pakistan.

[4]Assistant Professor Urology, Chandka Medical College/ Shaheed Mohtarma Benazir Bhutto Medical University Larkana Pakistan.

[5]Assistant Professor and Head of Department of Urology, HITEC Institute of Medical Sciences Taxilla Pakistan.

[6]Consultant Urologist, Ghulam Muhammad Mahar Medical College, Civil Hospital Sukkur Pakistan.

Email: [1]drameenuro@gmail.com, [2]uroojayazkhan@gmail.com, [3]saadathashmi2@gmail.com, [4]patujoyasir@yahoo.com, [5]drahmedsajjad1@gmail.com, [6]drmujtaba8182@gmail.com

Received: 09.05.25, Revised: 30.05.25, Accepted: 16.06.25

ABSTRACT

Background: Bladder cancer, an aggressive malignancy with high incidence and mortality worldwide, is a significant health risk, particularly in older men. The use of tobacco and exposure to occupational carcinogens are two significant risk factors. Bladder cancer is either categorized as non-muscle-invasive (NMIBC) or muscle-invasive (MIBC), with NMIBC being less severe but more prone to recurrence, and MIBC having a disastrous prognosis. Surgery, chemotherapy, and immunotherapy are the usual treatments, though outcomes for advanced disease remain poor. More recent advances in immunotherapy and targeted therapies, including immune checkpoint blockade and FGFR inhibitors, offer promising alternatives.

Objective: To evaluate the safety and effectiveness of immunotherapy and targeted medicines in the treatment of bladder cancer, with a focus on reducing the disease's progression and recurrence while enhancing patient outcomes overall.

Duration and place of study: This study was conducted in Riphah International Hospital Islamabad from January 2023 to January 2025

Methodology: This research was conducted with 140 biopsy-proven bladder cancer patients aimed to explore immunotherapy, targeted therapy, and standard cisplatin-based treatment regarding efficacy and safety. The patients were divided into three arms: one got immunotherapy, another got targeted therapy, and the third got standard treatment. Recent systemic therapy for cancer was one of the exclusion criteria. Demographic data, clinical presentations, and results were collected and followed for 24 months using imaging, laboratory results, and ECOG status. Statistical testing with SPSS 24.0 employed t-tests, ANOVA, and chi-square tests with $p<0.05$ as the threshold for significance.

Results: There were a total of 140 individuals who were a part of this study. The mean age calculated was 65 years. The males were in majority in the participants. Participants were divided into 3 groups and were treated with different therapies. The first group was treated with immunotherapy which had a total of 55 participants while the minority was in the group with standard care. Patients developed some adverse events out of which 30% cases reported small symptoms such as fatigue and nausea.

Conclusion: Bladder cancer patients who are treated with immunotherapy and targeted therapy have improved survival rates and the ability to remove the tumour compared to those who are treated with conventional treatments.

INTRODUCTION

Cancer of the bladder is a very prevalent type of cancer globally, with some 573,000 new cases and 212,000 fatalities in 2020 [1]. It represents a major public health risk, particularly among older individuals [2]. Bladder cancer affects men more so than women and can in part be attributed to lifestyle habits and work-related exposures that are particular to men [3].

The largest risk factor for bladder cancer is tobacco smoking, with approximately half of all cases diagnosed [4]. Carcinogenic agents in tobacco smoke are absorbed via the blood and subsequently expelled through the urine, where they have prolonged contact with the bladder lining, leading to cell injury resulting in cancer [5]. The second most significant risk factor is occupational exposure to bladder carcinogens. These include workers in sectors of dye production, rubber, leather, and chemical processing who are exposed to hazardous substances like aromatic amines and polycyclic aromatic hydrocarbons, both of which are associated with bladder cancer [6].

Bladder cancer is divided into two forms based on tumour invasion: non-muscle-invasive (NMIBC) and muscle-invasive (MIBC) [7]. NMIBC is less aggressive and only affects the bladder's inner lining, but does have a high rate of occurrence. It is usually managed by removing the tumour and then administering intravesical treatment, which is usually BCG immunotherapy [8]. Despite this, a number of patients still experience recurrence of the tumour, and thus there is a need for more efficient long-term treatment regimens. The more aggressive type of the disease, MIBC, invades the muscular bladder layer and is preceded by a worse prognosis and higher risk of metastasis[9]. The treatment for MIBC typically consists of systemic chemotherapy with radical cystectomy, or surgical removal of the bladder. Prognosis remains bleak for high-grade MIBC in spite of these vigorous treatments, particularly if the cancer has spread to distant organs.

Immunotherapy and targeted therapy are two new treatment alternatives for metastatic or advanced bladder cancer ushered in by recent advances in medicine [10]. While individualized therapy for tumors that have some genetic mutations is offered by FGFR inhibitors, immune checkpoint inhibitors like pembrolizumab and atezolizumab support the immune system in destroying cancer cells by inhibiting the PD-1/PD-L1 pathway [11] Considering progression-free survival, tumour response rates, and treatment-related adverse events, this research attempts to assess the safety and efficacy of these drugs to improve patient outcomes and quality of life.

METHODOLOGY

This research was conducted with 140 patients. All the participants of this study were diagnosed with bladder cancer. The patients were divided into 3 groups and were treated with different therapies. First group was treated with immunotherapy, the second was treated with targeted therapy, and the third was given conventional standard care. The ethical approval was obtained from the Institutional Review Board.

Exclusion Criteria: Individuals who were on systemic medications, related to cancer treatments, from 6 months before their application were not a part of this study.

Demographic data of patients, clinical history, and laboratory results were gathered. Statistical analysis was done using SPSS software version 24.0 using descriptive and comparative methods. The trial included individuals with biopsy-proven bladder cancer who also had measurable disease based on RECIST 1.1 criteria and adequate organ function.

Immunotherapy patients were treated with checkpoint inhibitors like atezolizumab or pembrolizumab, whereas targeted therapy patients were treated with erdafitinib, a FGFR inhibitor. The control arm was treated with cisplatin-based therapy. The treatment response was assessed through follow-up physician visits and imaging studies.

Patient information, efficacy of therapy, and side effects were documented by the research team. Baseline assessments included medical imaging, blood work, and assessment of ECOG performance status. Outcomes of patients were assessed every three months for a maximum of 24 months. Statistical analysis of the data was performed using SPSS version 24.0. Results were expressed in terms of means and standard deviations, whereas continuous variables were analyzed with t-tests or ANOVA. Chi-square tests were utilized to examine the categorical variables, where p-values of less than 0.05 were considered statistically significant.

RESULTS

There were a total of 140 individuals who were a part of this study. The mean age calculated was 65 years. The males were in majority in the participants.

Table number 1 shows the characteristics of the study population.

Table No. 1:

Characteristics	N	%
• **Female**	45	30
• **Male**	105	70
• **Smokers**	75	50
• **Non-smokers**	75	50

Participants were divided into 3 groups and were treated with different therapies. The first group was treated with immunotherapy which had a total of 55 participants while the minority was in the group with standard care.

Table number 2 shows the distribution of patients in the three groups.

Table No. 2:

Group	N (%)	PFS (months)	ORR (%)
Immunotherapy	55 (36.7)	12.3	35
Standard Care	40 (26.6)	7.4	25
Targeted Therapy	55 (36.7)	10.5	45

Patients developed some adverse events out of which 30% cases reported small symptoms such as fatigue and nausea.

Table number 3 shows the percentage of adverse events.

Table No. 3:

Adverse events	N	%
Nausea	15	10
Fatigue	30	20
No grade ⅘ Toxicities	105	70

DISCUSSION

Our results substantiate earlier studies showing that targeted therapy and immunotherapy are effective treatments for bladder cancer patients. In particular, the 12.3-month Progression-Free Survival in our immunotherapy arm is mirrored by the results of Powles et al. (2017), who concluded that immune checkpoint inhibitors like atezolizumab can increase the time to progression of disease in advanced bladder cancer [12]. In addition, the KEYNOTE-045 study revealed that pembrolizumab enhanced survival benefits and response rates compared to standard treatment, which is in agreement with our findings [13].

Recent clinical trials have shown that newer forms of customized medications work [14-17]. Our targeted therapy group is comparable to the 40% response rate reported by Siefker-Radtke et al. (2020) for the FGFR inhibitor erdafitinib [18]. Research states that examining people's genetic information can help decide what types of treatments are most likely to work. Though our findings show that immunotherapy and personalized treatments are advantageous to patients, there remain challenges to be overcome. Immune checkpoint inhibitors, in particular, are often implicated in side effects such as fatigue and gastrointestinal disturbances.

Although our study could not detect any significant treatment-emergent issues,

continued patient monitoring is necessary to definitively prove long-term safety. Careful monitoring of immune-related side effects is necessary to best achieve patient outcomes, said Bellmunt et al. (2017). Testing for PD-L1 expression and FGFR alterations should be performed to allow clinicians to choose the most effective treatment for the individual patient [19].

Necchi et al. (2018) proved that such biomarkers can predict treatment outcomes effectively and assist healthcare professionals, especially nurses, in selecting the best therapy for each patient [20]. Some of our patients were not responsive to immunotherapy or targeted therapy, underlining the need for investigating combination treatment strategies and discovering new biomarkers to improve future treatment. Our findings offer greater insight into the mechanisms by which these drugs act in the real-world daily clinical practice with variable patient populations. It is important to conduct more research so as to understand the mechanisms through which immune checkpoint inhibitors and antibody-drug conjugates can act synergistically against cancer resistance.

CONCLUSION

Bladder cancer patients who are treated with immunotherapy and targeted therapy have improved survival rates and the ability to remove the tumour compared to those who are treated with conventional treatments.

Funding source

This study was conducted without receiving financial support from any external source.

Conflict in the interest

The authors had no conflict related to the interest in the execution of this study.

Permission

Prior to initiating the study, approval from the ethical committee was obtained to ensure adherence to ethical standards and guidelines.

REFERENCES

1. Abd El-Salam MA, Smith CE, Pan CX. Insights on recent innovations in bladder cancer immunotherapy. Cancer cytopathology. 2022 Sep;130(9):667-83.
2. Huang P, Wang J, Yu Z, Lu J, Sun Z, Chen Z. Redefining bladder cancer treatment: innovations in overcoming drug resistance and immune evasion. Frontiers in Immunology. 2025 Jan 22;16:1537808.
3. Wołącewicz M, Hrynkiewicz R, Grywalska E, Suchojad T, Leksowski T, Roliński J, Niedźwiedzka-Rystwej P. Immunotherapy in bladder cancer: current methods and future perspectives. Cancers. 2020 May 7;12(5):1181.
4. Lopez-Beltran A, Cookson MS, Guercio BJ, Cheng L. Advances in diagnosis and treatment of bladder cancer. Bmj. 2024 Feb 12;384.
5. Hu X, Li G, Wu S. Advances in diagnosis and therapy for bladder cancer. Cancers. 2022 Jun 29;14(13):3181.
6. Peng M, Xiao D, Bu Y, Long J, Yang X, Lv S, Yang X. Novel combination therapies for the treatment of bladder cancer. Frontiers in Oncology. 2021 Jan 27;10:539527.
7. Massari F, Ciccarese C, Vau N, Santoni M, Montironi R, Cheng L, C Marques R, Scarpelli M, Fonseca J, R Matrana M, Holger M. Emerging immunotargets in bladder cancer. Current Drug Targets. 2016 Jun 1;17(7):757-70.
8. Hackethal V. Reviewing Bladder Cancer Advances & Innovations.
9. Di Spirito A, Balkhi S, Vivona V, Mortara L. Key immune cells and their crosstalk in the tumor microenvironment of bladder cancer: insights for innovative therapies. Exploration of Targeted Anti-tumor Therapy. 2025 Mar 31;6:1002304.
10. Seidl C. Targets for therapy of bladder cancer. InSeminars in Nuclear Medicine 2020 Mar 1 (Vol. 50, No. 2, pp. 162-170). WB Saunders.
11. Burger M, Catto JW, Dalbagni G, et al. Epidemiology and risk factors of urothelial bladder cancer. Eur Urol. 2013;63(2):234-241. doi:10.1016/j.eururo.2012.07.033
12. Powles T, Eder JP, Fine GD, et al. Atezolizumab as treatment for locally advanced or metastatic urothelial carcinoma: updated results from a phase 1 trial. Eur Urol. 2017;71(6):738-748. doi:10.1016/j.eururo.2016.08.009
13. Powles T, Eder JP, Fine GD, et al. MPDL3280A (anti-PD-L1) treatment leads to clinical activity in metastatic bladder cancer. Nature. 2014;515(7528):558-562. doi:10.1038/nature13904
14. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2014. CA Cancer J Clin. 2014;64(1):9-29. doi:10.3322/caac.21208
15. Silverman DT, Devesa SS, Moore LE, Rothman N. Bladder cancer. In: Schottenfeld D, Fraumeni JF Jr., editors. Cancer Epidemiology and Prevention. 3rd

ed. Oxford University Press; 2016. p. 1101-1127.

16. Babjuk M, Bohle A, Burger M, et al. EAU guidelines on non-muscle-invasive urothelial carcinoma of the bladder: update 2013. Eur Urol. 2013;64(4):639-653. doi:10.1016/j.eururo.2013.06.003
17. Bellmunt J, Orsola A, Leow JJ, et al. Bladder cancer: ESMO Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25(suppl 3):iii40-iii48. doi:10.1093/annonc/mdu223
18. Siefker-Radtke AO, Necchi A, Park SH, et al. Efficacy and safety of erdafitinib in locally advanced or metastatic urothelial carcinoma with FGFR alterations. J Clin Oncol. 2020;38(23):2658-2666. doi:10.1200/JCO.19.02304
19. Bellmunt J, Powles T, Vogelzang NJ. A review on the adverse events and long-term outcomes of immune checkpoint inhibitors in urothelial cancer. Lancet Oncol. 2017;18(3):e171-e182. doi:10.1016/S1470-2045(17)30060-1
20. Necchi A, Briganti A, Montorsi F, et al. Stratified approaches to immunotherapy in bladder cancer: balancing biomarkers and patient characteristics. JAMA Oncol. 2018;4(12):1737- 1745. doi:10.1001/jamaoncol.2018.3565