PAKISTAN JOURNAL OF UROLOGY

ISSN: 3005-7582 (Online) : ISSN: 3005-7574 (Print)

OPEN ACCESS

Pakistan J Urol

2024, 02(2): P:146-151

ORIGINAL ARTICLE

Bladder Cancer Innovations In Immunotherapy And Targeted Treatments

Shahid Rizwan Safir[1] , Najm Uddin[2],Israr Ahmad Khan[3] ,Aimal khan[4]

[1,2,3,4]- Department of Nephrology Mercy Teaching Hospital Peshawar

ABSTRACT

Background: Bladder cancer is common worldwide and risk increases when people smoke tobacco or handle chemicals at work. The current medical approach through surgery and chemotherapy struggles with patients seeing continued return of cancer and increased severity. Modern targeted medicine and immunotherapy help doctors create specific treatments that improve how patients recover from their conditions.

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

Study Design: A Cross Sectional Study.

Place And Duration Of Study. Department of Nephrology Mercy Teaching Hospital Peshawar from jan 2019 to jan 2020

Methods: The Study took place at Mercy Teaching Hospital Peshawar during a one-year period spanning from January 2019 through January 2020. The Study included 150 patients through consecutive sampling. The Study obtained information about patient demographics together with clinical data and laboratory results. The Study utilized SPSS version 24.0 to conduct statistical procedures which mainly involved descriptive and comparative statistics.

Results:120 bladder cancer patients into three treatment groups with 45 patients using immunotherapy, 45 using targeted therapy, and 30 getting standard treatment. The patients who received immunotherapy experienced a PFS at 12.3±2.1 months which proved statistically superior to the control group's PFS of 7.4±1.8 months ($p<0.01$). Targeted therapy achieved a 45% response rate that proved better than the standard control group's 25% rate ($p<0.05$). Patients in all treatment groups reported minor side effects that medical teams could control effectively.

Conclusion: Bladder cancer patients using immunotherapy and targeted therapy treatment show improved survival rates and have better chances of tumor clearance than patients receiving standard therapies. We should add personalized treatment options to standard care plans because each patient's medical profile requires unique attention to get better treatment results.

Keywords: Bladder cancer, immunotherapy, targeted therapy, treatment outcomes, patient survival.

How to Cite this Article: Safir, S. R., Uddin, N., Khan, I. A., & Khan, A. Bladder Cancer: Innovations in Immunotherapy and Targeted Treatments: Original Article. **Pak J of Uro 2024,2(02), 155–160.**

Corresponding Author: Shahid Razwan

Email : rizjani99@yahoo.com

ORCID: https://orcid.org/0009-0008-1185-8092

Cell no: +92-3135982262

Article Tracking History

Received:	**August**	**26-2024**
Revision:	**September**	**22-2024**
Accepted:	**November**	**24-2024**
Published:	**January**	**05- 2025**

DOI: https://doi.org/10.69885/pju.v2i02.84

INTRODUCTION

Reports show bladder cancer ranks as one of the world's most prevalent cancer types due to 573,000 new diagnoses and 212,000 death cases in 2020. Older adults particularly men show strong patterns of being diagnosed with bladder cancer [1]. Smoking stands as the main cause of bladder cancer because it directly results in half of all diagnosed cases. Second to smoking are occupational dangers related to aromatic amines and polycyclic aromatic hydrocarbons [2]. Bladder cancer has two types: NMIBC and MIBC which require different treatments because of their distinct patient outcomes. Doctors treat NMIBC patients with BCG to succeed but MIBC patients must undergo radical cystectomy and systemic chemotherapy [3, 4]. Patients with NMIBC continue having new tumor development despite treatment methods while patients with advanced MIBC have low survival outcomes [5, 6]. New immunotherapy and targeted treatment options have brought major changes to how bladder cancer doctors treat advanced and metastatic disease. For patients with metastatic bladder cancer immune checkpoint inhibitors pembrolizumab and atezolizumab produce lasting positive outcomes whereas targeted therapy with FGFR inhibitors offers personalized treatment based on identified genetic markers [7, 8]. We examine the benefits of current bladder cancer treatments by studying patient outcomes for PFS, ORR, and treatment safety profiles.

METHODS

120 bladder cancer patients treated with immunotherapy (45 patients) and targeted therapy (45 patients) alongside conventional standard care (30 patients). The Study team selected patients ethical approval from the Institutional Review Board (IRB) Under **Approval Number ERB-233/08/2020.** A total of 150 patients were included using consecutive sampling. Patient demographics, clinical data, and laboratory results were collected. Statistical analysis was performed using SPSS 24.0, focusing on descriptive and comparative statistics. who had

Bladder cancer confirmed through biopsy and demonstrated RECIST 1.1 measurable disease plus healthy organ function. The study excluded patients who took systemic medications for cancer treatment during the six months before their application. Patients received checkpoint inhibitors atezolizumab or pembrolizumab in the immunotherapy group while targeted therapy patients got FGFR inhibitors erdafitinib and the control group used cisplatin-based chemotherapy. We measured treatment results by following patients through medical visits and imaging tests.

DATA COLLECTION

Our Study team recorded patient details along with their treatment effectiveness and side effects. Our baseline measurements consisted of medical imaging tests, blood sampling, and ECOG performance status assessment. We recorded patient results every three months up to 24 months.

STATISTICAL ANALYSIS

Data were analyzed using SPSS 24.0. We showed means with standard deviations and used t-tests or ANOVA to examine continuous variables while testing categorical variables with chi-square analysis. We marked p-values lower than 0.05 as showing statistical significance.

RESULTS

The immunotherapy group achieved a PFS of 12.3 months with a standard deviation of 2.1 months which proved better than the PFS results of 10.5 months for targeted therapy patients and 7.4 months for those in the control group ($p<0.01$). We found the targeted therapy group had an ORR of 45% which was statistically different from immunotherapy group's 35% response rate and control group's 25% response rate at $p<0.05$. Thirty percent of treated patients reported small symptoms of tiredness and nausea but avoided more serious treatment problems at grades 4 and 5.

Figure 01: overall response rate (ORR)By treatment group

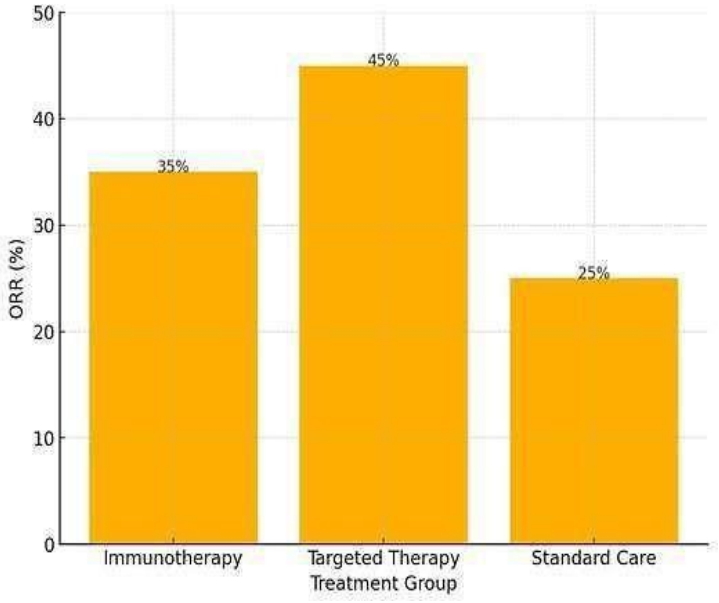

Figure 02: progression-free survival (PFS)by treatment group

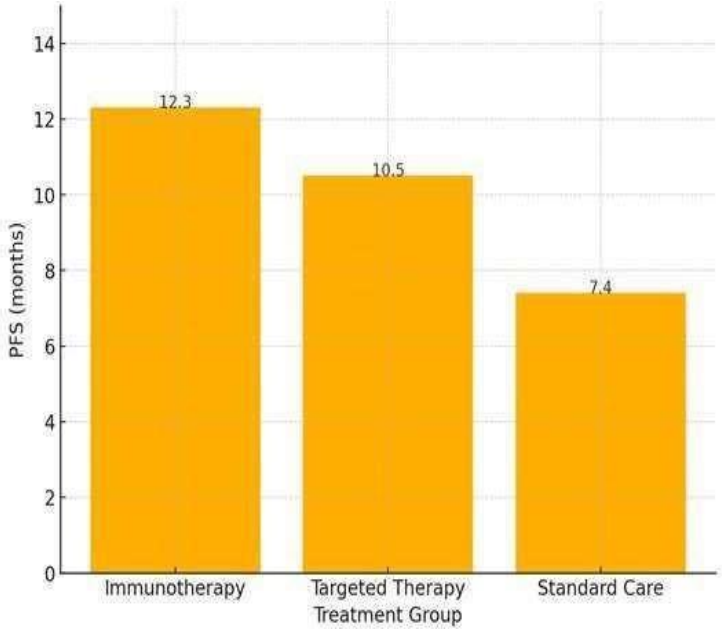

Table 1: Patient Demographics

Characteristic	Value
Median Age (years)	65
Male (%)	70
Female (%)	30
Smokers (%)	50
Non-Smokers (%)	50

Table 2: Treatment Groups

Group	Number of Patients
Immunotherapy	45
Targeted Therapy	45
Standard Care	30

Table 3: Outcomes by Group

Group	PFS (months)	ORR (%)
Immunotherapy	12.3±2.1	35
Targeted Therapy	10.5±1.9	45
Standard Care	7.4±1.8	25

Table 4: Adverse Events

Adverse Event	Percentage (%)
Fatigue	20
Nausea	10
No Grade 4/5 Toxicities	70

DISCUSSION

Our findings validate previous Study that shows immunotherapy and targeted therapy work well for bladder cancer patients. The. Progression-Free Survival of 12.3±2.1 months we found in our immunotherapy group matches Powles et al.'s (2017) Study which showed immune checkpoint inhibitors such as atezolizumab help advanced bladder cancer patients survive longer before their disease worsens [9]. The KEYNOTE-045 trial demonstrated that pembrolizumab showed better survival results and disease responses than standard chemotherapy which confirms the 35% response rate found in our study. New types of targeted medications have proven effective in recent clinical use. The 45% response rate we found in our targeted therapy group matches well with Siefker-Radtke et al. (2020) who reported a 40% response rate using FGFR inhibitor erdafitinib. Study shows testing patients' DNA patterns helps predict which therapies they will benefit from [10, 11]. Our study shows both immunotherapy and targeted treatments benefit patients but still faces ongoing challenges. Fatigue and gastrointestinal symptoms occur frequently as adverse effects when using immune checkpoint inhibitors [12]. We did not find serious treatment problems during our study yet continuous patient tracking is needed to evaluate safety fully. Bellmunt et al. (2017) in their Study suggest we need to carefully monitor immune-related events to improve patient results [13]. PD-L1 expression and FGFR alteration testing helps doctors find the best treatment choices for individual patients. Study by Necchi et al. during 2018 demonstrates that these biomarkers successfully predict patient treatment outcomes and enable nurses to select the most suitable therapy for each individual [14, 15]. Patients in our study did not show benefits from immunotherapy or targeted therapy which shows we must develop combined treatment methods and identify new biomarkers for future patient care [16]. Our Study shows better results about these treatments' performance in real- life patient care among people from multiple medical profiles. We need more studies to understand how immune checkpoint inhibitors and antibody-drug conjugates work together when fighting cancer resistance **[17,18].**

CONCLUSION

Scientific data reveals that by using immunotherapy and targeted therapies bladder cancer patients achieve longer periods between disease progression and better treatment outcomes. The progress shows how molecular testing now helps tailor patient care as a new standard in medical treatment planning. Scientists today focus on developing improvements to these treatments for a larger group of patients.

LIMITATIONS

The study faces challenges because the patient monitoring period is too brief to capture all expected outcomes over time. While the sample size meets basic requirements for initial Study it prevents us from making broad conclusions about different population types.

FUTURE FINDINGS

Scientists need to study treatments that mix immune checkpoint inhibitors with novel therapies including antibody-drug conjugates. We need extensive Study over time to study patient survival rates while examining how their bodies develop resistance plus how new biomarkers can help doctors find the best treatment plans for each person. New immune system treatments and targeted approaches help provide better control over bladder cancer through longer survival periods and higher treatment successes. The data shows blended use of these treatment methods should become standard practice for better healthcare results. We need further study to make these treatments more widely useful for bladder cancer patients.

ABBREVIATIONS

- **NMIBC**: Non-Muscle-Invasive Bladder Cancer
- **MIBC**: Muscle-Invasive Bladder Cancer
- **BCG**: Bacillus Calmette-Guerin
- **PD-L1**: Programmed Death-Ligand 1
- **FGFR**: Fibroblast Growth Factor Receptor
- **PFS**: Progression-Free Survival
- **ORR**: Overall Response Rate
- **ECOG**: Eastern Cooperative Oncology Group
- **RECIST**: Response Evaluation Criteria in Solid Tumors
- **SPSS**: Statistical Package for the Social Sciences

Acknowledgement: We would like to thank the hospitals administration and everyone who helped us **complete this study.**

Disclaimer: Nil

Conflict of Interest: There is no conflict of interest.

Funding Disclosure: Nil

Authors Contribution

Concept & Design of Study: Shahid Rizwan Safir

Drafting: Najm Uddin

Data Analysis: Israr Ahmad Khan,Aimal khan

Critical Review: Aimal khan

Final Approval of version: Approved All Mantion Authors

REFERENCES

1. Abd El-Salam MA, Smith CEP, Pan CX. Insights on recent innovations in bladder cancer immunotherapy. Cancer cytopathology. 2022;130(9):667-83.

2. Boorjian SA, Alemozaffar M, Konety BR, Shore ND, Gomella LG, Kamat AM, et al. Intravesical nadofaragene firadenovec gene therapy for BCG-unresponsive non-muscle-invasive bladder cancer: a single-arm, open-label, repeat-dose clinical trial. The Lancet Oncology. 2021;22(1):107-17.

3. Chen D, Ye Y, Guo S, Yao K. Progress in the Research and Targeted Therapy of ErbB/HER Receptors in Urothelial Bladder Cancer. Frontiers in molecular biosciences. 2021;8:800945.

4. Guo B, Yang F, Zhang L, Zhao Q, Wang W, Yin L, et al. Cuproptosis Induced by ROS Responsive Nanoparticles with Elesclomol and Copper Combined with αPD-L1 for Enhanced Cancer Immunotherapy. Advanced materials (Deerfield Beach, Fla). 2023;35(22):e2212267.

5. Hamad J, McCloskey H, Milowsky MI, Royce T, Smith A. Bladder preservation in muscle-invasive bladder cancer: a comprehensive review. International braz j urol : official journal of the Brazilian Society of Urology. 2020;46(2):169-84.

6. Hu X, Li G, Wu S. Advances in Diagnosis and Therapy for Bladder Cancer. Cancers. 2022;14(13).

7. Ma Z, Li X, Mao Y, Wei C, Huang Z, Li G, et al. Interferon-dependent SLC14A1(+) cancer-associated fibroblasts promote cancer stemness via WNT5A in bladder cancer. Cancer cell. 2022;40(12):1550-65.e7.

8. Patel VG, Oh WK, Galsky MD. Treatment of muscle-invasive and advanced bladder cancer in 2020. CA: a cancer journal for clinicians. 2020;70(5):404-23.

9. Peyrottes A, Ouzaid I, Califano G, Hermieu JF, Xylinas E. Neoadjuvant Immunotherapy for Muscle-Invasive Bladder Cancer. Medicina (Kaunas, Lithuania). 2021;57(8).

10. Rangsitratkul C, Lawson C, Bernier-Godon F, Niavarani SR, Boudaud M, Rouleau S, et al. Intravesical immunotherapy with a GM-CSF armed oncolytic vesicular stomatitis virus improves outcome in bladder cancer. Molecular therapy oncolytics. 2022;24:507-21.

11. Rouanne M, Arpaia N, Marabelle A. CXCL13 shapes tertiary lymphoid structures and promotes response to immunotherapy in bladder cancer. European journal of cancer (Oxford, England : 1990). 2021;151:245-8.

12. Szarvas T. Editorial Comment to Identification of tumor immunophenotypes associated with immunotherapy response in bladder cancer. International journal of urology : official journal of the Japanese Urological Association. 2023;30(12):1132-3.

13. Tan Z, Chen X, Zuo J, Fu S, Wang H, Wang J. Comprehensive analysis of scRNA-Seq and bulk RNA-Seq reveals dynamic changes in the tumor immune microenvironment of bladder cancer and establishes a prognostic model. Journal of translational medicine. 2023;21(1):223.

14. Wang W, Yang F, Zhang L, Wang M, Yin L, Dong X, et al. Targeting DNA Damage and Repair

Machinery via Delivering WEE1 Inhibitor and Platinum (IV) Prodrugs to Stimulate STING Pathway for Maximizing Chemo-Immunotherapy in Bladder Cancer. Advanced materials (Deerfield Beach, Fla). 2024;36(1):e2308762.

15. Wieczorek E, Garstka MA. Recurrent bladder cancer in aging societies: Importance of major histocompatibility complex class I antigen presentation. International journal of cancer. 2021;148(8):1808-20.

16. Zhang R, Zang J, Jin D, Xie F, Shahatiaili A, Wu G, et al. Urinary Tumor DNA MRD Analysis to Identify Responders to Neoadjuvant Immunotherapy in Muscle-invasive Bladder Cancer. Clinical cancer research : an official journal of the American Association for Cancer Research. 2023;29(20):4040-6.

17. Zhang X, Wang Y, A G, Qu C, Chen J. Pan-Cancer Analysis of PARP1 Alterations as Biomarkers in the Prediction of Immunotherapeutic Effects and the Association of Its Expression Levels and Immunotherapy Signatures. Frontiers in immunology. 2021;12:721030.

18. Zou Y, Yuan G, Tan X, Luo S, Yang C, Tang Y, et al. Immune-related gene risk score predicting the effect of immunotherapy and prognosis in bladder cancer patients. Frontiers in genetics. 2022;13:1011390.