

Original Research Article

A prospective study on the role of immunotherapy in metastatic cancer patients at Combined Military Hospital Dhaka

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Received: 26 February 2023

Accepted: 13 March 2023

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ABSTRACT

Background: Immunotherapy is a treatment that uses a person's immune system to fight cancer. Immunotherapy can boost or change how the immune system works so it can find and attack cancer cells. Among several cancers, metastatic cancer causes high mortality, and immunotherapies are expected to be effective in the prevention and treatment of metastatic cancer patients. In Bangladesh, we do have not enough research-based information regarding the role of immunotherapy in treating metastatic cancer patients. This study aimed to assess the role of immunotherapy in treating metastatic cancer patients.

Methods: This prospective observational study was conducted in combined military hospital Dhaka, Bangladesh during the period from 26 March 2021 to 21 July 2022. In total 19 patients with metastatic cancer were enrolled in this study as study subjects. Proper written consent was taken from all the participants before data collection. Two (02) different outcomes were studied in this study; progression-free survival (PFS) and side effect percentages. A predesigned questionnaire was used in data collection. All data were processed, analyzed, and disseminated by using MS excel and SPSS version 23 program as per necessity.

Results: In using pembrolizumab, side effects, fatigue, nausea, and decreased appetite were found 43%, 22%, and 20% lesser respectively than chemotherapy which was noticeable. In using nivolumab, as a side effect, skin rash was found 66% lesser than chemotherapy. Besides this, itching, face swelling, and apnea was found 33% lesser. On the other hand, in using atezolizumab, as side effects, swelling of arms and constipation were found 66% lesser, and itching, as well as apnea, was found 33% lesser than that in chemotherapy. At the 6-month follow-up we observed that in the nivolumab and atezolizumab treated groups 66% of cases survived separately whereas, in pembrolizumab treated group, 61% survived.

Conclusions: In this study in all treatment groups, side effects were found as lesser than that in using chemotherapy. No major complication of any patients was observed in this study. So, can conclude that immune checkpoint inhibitors (ICIs) are better choice for metastatic diseases and ICIs exert lesser side effects than conventional chemotherapies.

Keywords: Role, Immunotherapy, Metastatic cancer, Pembrolizumab, Nivolumab, Atezolizumab

INTRODUCTION

Cancer is a genetic disease, with the growth of tumor cells initiated as well as promoted by mutations in a group of genes. This is just the beginning of a process of cancerogenesis, characterized by cellular, genetic as well as epigenetic alterations and the loss of normal cellular regulatory processes.¹ The set of all mutations

(Mutanome) gradually increases and leading to the heterogeneity of tumor cells and the synthesis of novel proteins and peptide sequences or neoantigens.² Immunotherapy is a type of treatment that exploits a patient's immunological system to cure a disease, including cancer. For many decades, the possible role of the immune system in cancer treatment remained unappreciated, not only due to a lack of appropriate

analytic techniques but also because of the undoubtedly disabled function of the host immunological response against the tumor.³ It was also revealed that mice with syngeneic carcinogen-induced tumors are resistant to redeveloping tumors with the same cancer cells because of the development of adaptive tumor immunity.⁴ In the 1970s, it was verified that tumor-derived T-cell clones recognize the human tumor cell lines and correlate with adaptive immunity.⁵ In 1980s, a detailed conformation of tumor neoantigens was revealed with the help of the newly introduced cloning techniques.⁶ It was also described that antigens are tumor-specific and highly immunogenic, they are not subject to central tolerance.⁷ In recent years, the progress in cancer immunotherapy has increased. In year of 2012, scientists discovered that the immune response in cancer is a series of carefully regulated events that may be optimally addressed not separately, but as a group.⁸ But the defective immune protection in cancer patients results from inhibiting T cell responses by negative regulators in lymphoid organs (checkpoints).⁹ Besides this, approach based on increasing the immunological activity of patients poses a threat in the form of autoimmune inflammatory responses, which cannot be ignored.¹⁰ Although, it seems that, in shared antigenic targets such as on-target, off-tumor toxicity is unavoidable and increases with the avidity, though some studies disagree with this opinion.¹⁶ The main objective of this study was to assess the role of immunotherapy in treating metastatic cancer patients.

METHODS

This prospective observational study was conducted in combined military hospital Dhaka, Bangladesh during the period from 26 March 2021-21 July 2022. In total 19 patients with metastatic cancer were enrolled in this study as study subjects. Properly written consent was taken from all the participants before data collection. Study was approved by ethical committee of mentioned hospital. Proper written consent taken from all participants before data collection. Whole intervention was conducted under the principles of human research specified in the Helsinki declaration and executed in compliance with currently applicable regulations and the provisions of the general data protection regulation (GDPR).^{14,15} In this study, 3 widely used ICIs were applied. Those were ‘pembrolizumab-PD-1 inhibitor, nivolumab-PD-1 inhibitor, and atezolizumab-PD-L1 inhibitor.

In the majority of the patients (n=13), pembrolizumab was applied. On the other hand, Nivolumab and atezolizumab were applied in the other 2 groups containing 3 patients in each. All the demographic and clinical data of the participants were recorded. Two (02) different outcomes were studied in this study; progression-free survivals (PFS) and side effect percentages. A predesigned questionnaire was used in data collection. All data were processed, analyzed, and disseminated by using MS excel and SPSS version 23 program as per necessity.

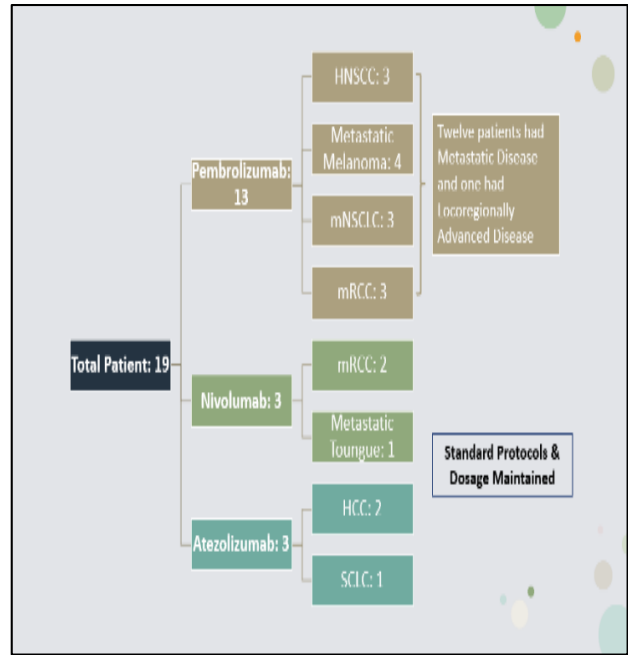


Figure 1: Patient details regarding immunotherapy, (n=19).

RESULTS

This prospective observational study was conducted in combined military hospital Dhaka, Bangladesh during the period from 26 March 2021 to 21 July 2022. In total 19 patients with metastatic cancer were enrolled in this study as study subjects. Among the total of 19 participants, as ICIs, pembrolizumab was applied in 68% (n=13) cases. Besides those, nivolumab and atezolizumab were applied in the other 2 groups containing 3 (16%) patients in each. In Pembrolizumab treated group, the highest number of patients (21%) with metastatic melanoma. Besides those, cases with head and neck squamous cell carcinoma, metastatic non-small-cell lung cancer, and metastatic renal cell cancer were 16% separately. In nivolumab treated group, cases with metastatic renal cell cancer contributed 11% and cases with metastatic tongue were 1 in number (5%). On the other hand, in atezolizumab treated group, cases with hepatocellular carcinoma were 11% and cases with small cell lung cancer were 1 in number (5%). In this study in all the treatment groups, side effects were found as lesser than that in using chemotherapy. In using pembrolizumab, side effects, fatigue, nausea, and decreased appetite were found 43%, 22%, and 20% lesser respectively than chemotherapy which was noticeable. In using nivolumab, as a side effect, skin rash was found 66% lesser than chemotherapy. Besides this, itching, face swelling, and apnea was found 33% lesser. On the other hand, in using atezolizumab, as side effects, swelling of arms and constipation were found 66% lesser, and itching, as well as apnea, was found 33% lesser than that in chemotherapy. At the 6-month follow-up we observed that in the nivolumab and atezolizumab treated groups

66% of cases survived separately whereas, in pembrolizumab treated group, 61% survived.

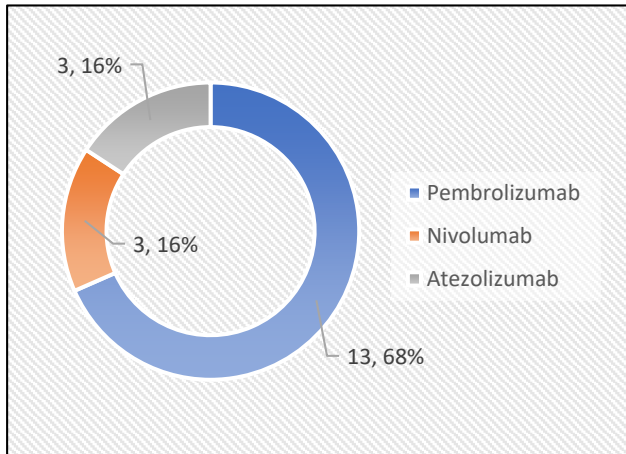


Figure 1: ICIs distribution among participants, (n=19)

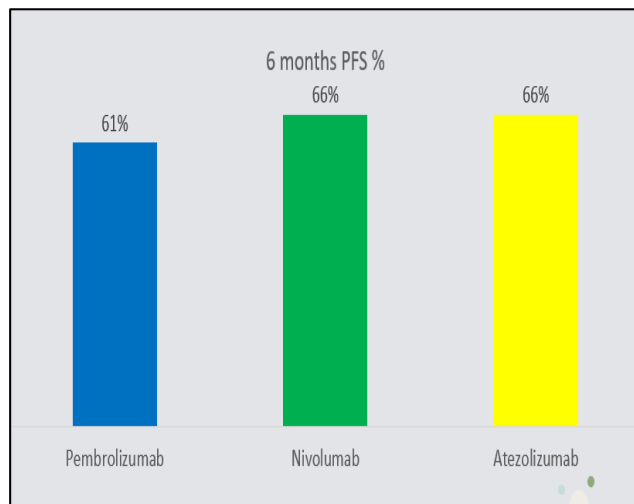


Figure 2: Progressing free survivals among participants, (n=19).

Table 1: Diseases status-wise ICSS distribution (n=19).

Disease type	N	Percentages (%)
Pembrolizumab		
HNSCC	3	16
Metastatic melanoma	4	21
mNSCLC	3	16
mRCC	3	16
Nivolumab		
mRCC	2	11
Metastatic tongue	1	5
Atezolizumab		
HCC	2	11
SCLC	1	5

HNSCC: head and neck squamous cell carcinoma; mNSCLC: Metastatic non-small-cell lung cancer; mRCC: Metastatic renal cell cancer; HCC: Hepatocellular carcinoma; SCLC: small cell lung cancer.

Table 2: Lesser side effects than chemotherapy in treating by pembrolizumab (n=13).

Side effects	Percentages (%)
Fatigue	43
Nausea	22
Decreased appetite	20
Myalgia	11
Peripheral neuropathy	1.7

Table 3: Lesser side effects than chemotherapy in treating by nivolumab (n=3).

Side effects	Percentages (%)
Skin rash	66
Itching	33
Face swelling	33
Apnea	33

Table 4: Lesser side effects than chemotherapy in treating by atezolizumab (n=3).

Side effects	Percentages (%)
Swelling of arms	66
Decreased appetite	33
Constipation	66
Hair loss	33

DISCUSSION

This study aimed to assess the role of immunotherapy in treating metastatic cancer patients. In this study, in pembrolizumab treated group, the highest number of patients (21%) were with metastatic melanoma. Besides those, cases with head and neck squamous cell carcinoma, metastatic non-small-cell lung cancer, and metastatic renal cell cancer were 16% separately. In Nivolumab treated group, cases with metastatic renal cell cancer contributed 11% and cases with metastatic tongue were 1 in number (5%). On the other hand, in atezolizumab treated group, cases with hepatocellular carcinoma were 11% and cases with small cell lung cancer were 1 in number (5%). A recent study of patients with advanced solid tumors demonstrated that TMB of greater than 10 was associated with an increased response rate to pembrolizumab monotherapy regardless of microsatellite status.¹⁴ A Japanese nivolumab using trial study found a response rate of 33% and a median progression-free survival (PFS) of 7.9 months among 24 patients with MSS metastatic cancer who had disease progression with standard chemotherapy.¹⁵ In this study in all the treatment groups, side effects were found as lesser than that in using chemotherapy. In using pembrolizumab, side effects like fatigue, nausea, and decreased appetite were found 43%, 22%, and 20% lesser respectively than chemotherapy which was noticeable. In using nivolumab, side effect such as skin rash was found 66% lesser than chemotherapy. Besides this, itching, face swelling, and apnea was found 33% lesser. On the other hand, in using atezolizumab, as side effects, swelling of

arms and constipation were found 66% lesser, and itching, as well as apnea, was found 33% lesser than that in chemotherapy. At the 6-month follow-up we observed that in the nivolumab and atezolizumab treated groups 66% of cases survived separately whereas, in pembrolizumab treated group, 61% survived. The clinical benefits experienced from nivolumab, pembrolizumab, and atezolizumab in prior studies have been consistent and are not likely to alter our findings substantially.¹⁶⁻¹⁸ All the findings of this study may be helpful for similar further studies and in the treatment arena of metastatic cancer.

Limitations

Cardiotoxicity, hepatotoxicity, blood-related toxicity, nephrotoxicity, and severe vomiting were not observed. This was a single-centered study with small-sized samples. Moreover, the study was conducted over a very short period. So, the findings of this study may not reflect the exact scenario of the whole country.

CONCLUSION

In this study in all the treatment groups, side effects were found as lesser than that in using chemotherapy. No major complication of any patients was observed in this study. So, we can conclude that ICIs are a better choice for metastatic diseases and ICIs exert lesser side effects than conventional chemotherapies. For getting more specific results, we would like to recommend conducting similar studies in several places with larger-sized samples.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Elahi MQE. A prospective study on the role of immunotherapy in metastatic cancer patients at Combined Military Hospital Dhaka. *Int J Res Med Sci* 2023;11:1056-9.