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ORIGINAL ARTICLE

Pembrolizumab and Chemotherapy with Radiology Comparative Analysis in Patients with Untreated Metastatic Triple Negative Breast Cancer

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ABSTRACT

Objective: This research compares the results of radiography, chemotherapy, and pembrolizumab usage in patients with metastatic triple-negative breast cancer who have not previously received any treatment.
Study Design: Observational/Comparative study.
Place and Duration: Sadiq Abbasi Hospital Bahawalpur. November 2021-May 2022
Methods: 100 females between the ages of 20 and 80 participated in this study. Included were patients with metastatic triple-negative breast cancer who had not yet begun therapy. Patients were split into two groups equally. 50 patients in group A got pembrolizumab 200 mg every two weeks while 50 patients in group B got chemotherapy (75 mg of Adriamycin) every 21 days for six months. Patients were followed up with often. Post-treatment results for both groups were evaluated and contrasted with regard to effectiveness, disease control, mortality, and recurrence rate. The full set of data was analyzed using SPSS 20.0.
Results: We found that efficacy in group A was higher in 22 (44%) cases as compared to group B in 15 (30%) cases. Frequency of partial recovery in both groups were 14 (28%) and 10 (20%). Frequency of stability in disease among patients of group B was higher 16 (32%) as compared to group A 9 (18%). Mortality and recurrence rate was lower in pembrolizumab group as compared to chemotherapy group with p value <0.004. Frequency of adverse outcomes in group A was higher.
Conclusion: We came to the conclusion from this study that the usage of pembrolizumab injection for the breast cancer treatment was beneficial and successful in terms of low mortality with recurrence rate and greater number of recovery, although rate of stability among illness was higher in chemotherapy group. Decreased illness rate was achieved with both therapies.
Keywords: Mortality, Chemotherapy, Recurrence, Pembrolizumab, Breast Cancer

INTRODUCTION

The paradigm of treatment for cancer has been altered by immunotherapy, and this has opened up new opportunities for study. Many active clinical studies are evaluating the effectiveness of next-generation immunotherapy medicines, novel indications, and combination treatments. Over the past ten years, the US United states Food And drug (FDA) has authorised a number of immune checkpoint inhibitors to treat cancer. The cell cycle death 1 (PD-1) inhibition pembrolizumab, immunotherapy, and cemiplimab, the programmed death alkene 1 (PD-L1) inhibition atezolizumab, durvalumab, and avelumab, and the cytotoxic T lymphocyte-associated protein 4 (CTLA-4) receptor immunotherapy are among the checkpoint inhibitors that are currently approved for use. When immune cells or tumour cells are both positive for the PD-L1 ligand, which normally attaches to PD-1 on Th1 to prevent the immune system from clearing tumour cells, these drugs can produce a long-lasting response. PD-1/PD-L1 drugs prevent this interaction, enabling the immune system to identify and destroy tumour cells. The interaction of CTLA-4 on T lymphocytes and its ligands CD86 and Co - stimulatory molecules on cortical antigen-presenting cells, which ordinarily suppresses T lymphocyte response, is another method of tumour immune evasion. Immediately after using the CTLA-4 inhibitor .[1]

In the treatment of advanced PD-L1-positive quintuple breast cancer (TNBC), the FDA granted expedited clearance to the anti-PD-L1 drug chronic medical conditions and the anti-PD-1 drug pembrolizumab based on advancement survival (PFS). These regimens underwent first-line evaluation .[2]

PD-1 (configurable death receptor 1) is a route that cancer cells might use to avoid being found by the immune system [3]. PEMBOLIZUMAB, a highly selective humanised monoclonal of the form IgG4-j subclass, inhibits the interaction between immune response proteins PD-1 as well as their receptor ligands, including such PD-L1 and PD-L2. About 50% of breast cancers have been reported to express PD-L1, with TNBC expressing it much more than normal tissue [4]. In the stage Ib KEYNOTE-012 trial, individuals with PD-L1 metastatic TNBC who had previously received treatment showed tolerable tolerability and antitumor effectiveness (N 14 32). Long-term pembrolizumab medication had been administered to these individuals. [5]

When especially in comparison to breast cancer survivors with a Charlson Comorbidity Index (CCI) score of 0, the Comorbidity Index (CCI) evaluations of 1, 2, and >3 recommended that cancer survivors with rising chronic conditions had an increased probability of quasi disposition, longer hospitalisation, and in-patient death. Comorbid conditions like high blood pressure and diabetes increase the likelihood that breast cancer survivors would experience unfavourable results from their therapy. Comorbidities have a negative effect on the quality of life for breast cancer survivors. The life quality for survivors of breast carcinoma is becoming an increasingly crucial criterion, thus I believe this is a subject that needs to be further investigated [6, 7]. Cancer mortality rates and durations are rising.

The effect of comorbidities on the quality of life of breast cancer survivors has not been identified by studies using self-reported data. .. Deshpance and associates [7] investigated the quality of life of breast cancer patients one year after diagnosis. According to Katz's study of comorbidity, breast cancer survivors who had more chronic diseases had worse physical and psychological performance. In the situation of 66% of patients without a burden of chronic disease, symptoms of a concurrent illness had to be determined by having patients soul their symptoms. Smith and colleagues examined the relationship between comorbid illnesses, cancer, and wellness life quality (HRQOL) in a study of older people with cancer [8]. The quality of life was poorer for breast cancer survivors who had two or more comorbidity, particularly if they had been diagnosed recently. The quality of life of breast cancer survivors is significantly impacted by medically diagnosed comorbidities before and after treatment, as well as by the patterns for comorbidity development and their effects on survivors' quality of life.

Pembrolizumab was used as a monotherapy in two groups of people with mTNBC who have been recruited in the KEYNOTE-086 investigation. A total of 170 patients with previously treated mTNBC and PD-L1 expression from Cohort A were included. The ORR for pembrolizumab was 5.3%, and the side effects in this situation were well-managed; [7–10] The addition of previously untreatable significantly increased median PFS especially in comparison with chemotherapeutics alone in both the ideation inhabitants (7.2 vs 5.5 months, in both, P = 0.002) and the PD-L1+ sub - group of sick people (7.5 vs 5.0 months, P 0.001) in a

randomised, phase III clinical trial in those who had previously untreated advanced TNBC[9]. This improvement was associated with a clinically meaningful improvement in overall survival .[10]

Our trial, which compares the effects of treatment with radiology/chemotherapy and the use of pembrolizumab, will be focused on patients with untreated metastatic triple-negative breast cancer that is PD-L1 positive.

MATERIAL AND METHODS

This comparative study was conducted at Sadiq Abbasi Hospital Bahawalpur and comprised of 100 patients. After receiving informed written consent, the demographic information of the recruited cases, including age, BMI, co-morbidities, and literacy, was computed. Patients with a history of chemotherapy, those under the age of 20, and those who did not provide written consent were removed from this research.

Patients ranged in age from 20 to 80. Included patients with metastatic triple-negative breast cancer who had not yet started therapy. Only recently acquired cores or tumor resection biopsy (recommended) or archive tumour material from a quasi lesion may be utilised for central confirmation to verify TNBC status and ascertain the status of PD-L1. For six months, 50 patients in group A got pembrolizumab 200 mg each two weeks, whereas 50 patients in group B received chemotherapy (75 mg of Adriamycin) every 21 days. Treatment was discontinued due to disease progression, intolerable toxicity, a doctor's choice or a patient's reluctance to cooperate. Until the subsequent imaging scan, three weeks later, reveals radiologic progression, individuals who are medically fit but have radiologic evidence of progression of the disease can continue therapy. At the start of the trial, every six weeks for the first 6 months, then every 4 weeks for the remaining six months, CT or MRI scans were performed. In a lab setting, PD-L1 expression was examined.

Vital signs were regularly checked during the research as well as at various times throughout the physical exam and laboratory testing. The effectiveness, disease control, mortality, and recurrence rate of post-treatment outcomes for the two groups were evaluated and compared. The entire data set was analyzed using SPSS 20.0. There was a mean standard deviation. By using frequencies and percentages, categorical variables were evaluated.

RESULTS

Among all cases, 13 (13%) cases had age 21-30 years, 23 (23%) cases had age 31-40 years, 36 (36%) cases were aged between 41-50 years and 28 (28%) patients had age >50 years.(figure 1)

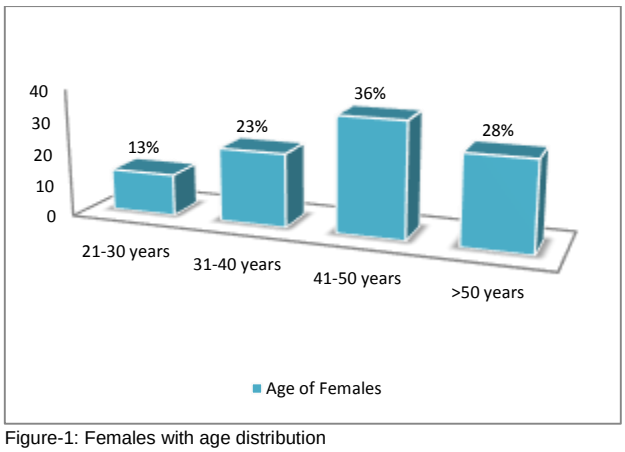

Figure-1: Females with age distribution

Majority of the patients 73 (73%) had BMI >25kg/m^2. Among 130 cases, 54 (54%) patients were educated and 59 (59%) cases were from rural areas. Diabetes mellitus, hypertension, arthritis, heart disease and chronic kidney disease were the comorbidities .(table 1)

Table 1: Included females with baseline details

Variables	Frequency	Percentage
BMI		
>25kg/m^2	73	73
<25kg/m^2	27	27
Literacy		
Educated	54	54
Non-educated	46	46
Place of Resident		
Rural	59	59
Urban	41	41
Other Diseases		
DM	35	35
HTN	30	30
Arthritis	17	17
IHD	10	10
CKD	8	8

We found that efficacy in group A was higher in 22 (44%) cases as compared to group B in 15 (30%) cases. Frequency of partial recovery in both groups were 14 (28%) and 10 (20%). Frequency of stability in disease among patients of group B was higher 16 (32%) as compared to group A 9 (18%).(figure 2)

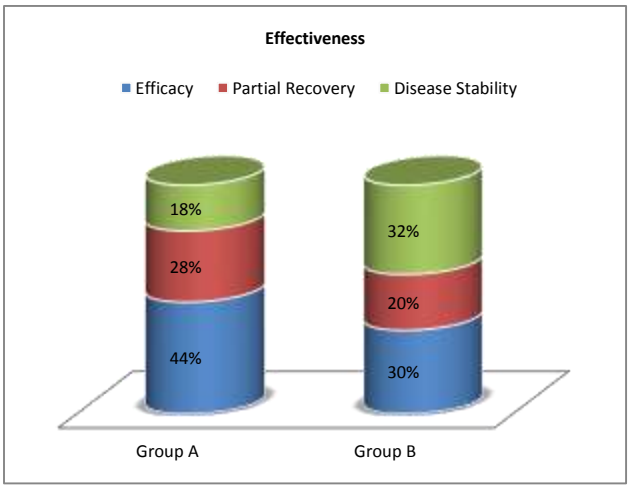

Figure-2: Comparison of efficacy among both groups

Mortality 7 (7%) and recurrence rate 3 (3%) was lower in pembrolizumab group as compared to chemotherapy group (16% and12%) with p value <0.004.(table 3)

Table 3: Recurrence and mortality among both groups

Variables	Group A (50)	Group B (50)
Outcomes		
Mortality	3 (6%)	8 (16%)
Recurrence	2 (4%)	6 (12%)

Table 4: Association of complication among both groups

Variables	Group A (50)	Group B (50)
Complications of treatment		
Fatigue	12 (24%)	9 (18%)
Nausea	11 (22%)	7 (14%)
Diarrhea	5 (10%)	6 (12%)
Anemia	2 (4%)	5 (10%)
Pruritus	1 (2%)	2 (4%)
Complications of Immune-mediated		
Hypothyroidism	5 (10%)	3 (6%)
Hyperthyroidism	3 (6%)	3 (6%)
Pneumonitis	1 (2%)	4 (8%)
Adrenal insufficiency	3 (6%)	2 (4%)
Colitis	2 (4%)	1 (2%)

We found negative outcomes in both groups that were connected to therapy and infusion. When compared to the chemotherapy group, the frequency of side effects was considerably greater in the pembrolizumab group.(table 4)

DISCUSSION

In patients having PD-L1-positive mTNBC who had never previously had treatment for metastatic illness, pembrolizumab monotherapy showed an acceptable safety profile. In a limited sample of people with previously treated mTNBC, pembrolizumab monotherapy demonstrated antitumor efficacy. Pembrolizumab avoided frequent chemotherapy side effects and delivered long-lasting outcomes, despite a lower ORR than solitary chemotherapy (5.3 percent). For individuals who were PD-L1 positive, pembrolizumab as the initial line of therapy had a significant, long-lasting anticancer impact.[11]

Pembrolizumab strong work ethic, durable antitumor effect as first-line therapy for PD-L1-positive mTNBC in addition to the manageable safety profile; the ORR of 21.4% after one median follow-up of 12.3 months was comparable to that observed with solitary chemotherapies as first-line therapy for mTNBC.[12]

In our study, diabetes mellitus, hypertension, arthritis, heart disease and chronic kidney disease were the comorbidities. It is crucial to assess the effect on patients' life quality because the majority of people have been identified with at most one of the comorbidities. These results concurred with those of earlier research.[13]

In present study, efficacy in group A was higher in 22 (44%) cases as compared to group B in 15 (30%) cases. Frequency of partial recovery in both groups were 14 (28%) and 10 (20%). Frequency of stability in disease among patients of group B was higher 16 (32%) as compared to group A 9 (18%). A recent trial from Pakistan found that injectable pembrolizumab was a helpful and successful monotherapy among individuals with PD-L1-positive mTNBC, with fewer negative effects and a greater rate of effectiveness. [14] Similar outcomes have been shown in studies utilising immune checkpoint inhibitors to treat mTNBC. In the KEYNOTE-012 study, pembrolizumab was used to treat 32 patients with mTNBC. Results showed an ORR of 18.5%, a mean latency to reaction of 4.1 months, and an extended median response duration (within 3.4 and 10.9 months).[15]

We found that mortality 7 (7%) and recurrence rate 3 (3%) was lower in pembrolizumab group as compared to chemotherapy group (16% and12%) with p value <0.004.[16] We found negative outcomes in both groups that were connected to therapy and infusion. When compared to the chemotherapy group, the frequency of side effects was considerably greater in the pembrolizumab group.[17]

Age has been shown to be a significant consideration when selecting cancer treatments, particularly chemotherapy, due to worries about comorbidity and drug toxicity.[18] The lowered effectiveness of chemotherapy for breast cancer with era may have changed the knowledge and attitudes of oncologists and patients about the advantages and risks of chemotherapy for women with breast cancer as they grew older. Contrary to male and female with colon cancer, chemotherapy efficiency and efficacy do not decrease with age in female with breast cancer.[19] According to our trial, pembrolizumab monotherapy was typically well tolerated in patients with PD-L1-positive mTNBC who had not previously received treatment. A level 3 AE as a consequence of therapy was only experienced by 24% of individuals. For individuals with PD-L1-positive mTNBC, pembrolizumab monotherapy as first-line therapy showed a tolerable safety profile and sustained anticancer efficacy.

CONCLUSION

We came to the conclusion from this study that the usage of pembrolizumab injection for the breast cancer treatment was beneficial and successful in terms of low mortality with recurrence rate and greater number of recovery, although rate of stability among illness was higher in chemotherapy group. Decreased illness rate was achieved with both therapies.

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