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ORIGINAL ARTICLE

Comparative Analysis of Pembrolizumab and Chemotherpay with Radiology Among Patients of Untreated Pd-L1 Positive Metastatic Triple Negative Breast Cancer

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ABSTRACT

Objective: The aim of this study is to compare the outcomes of chemotherapy with radiology and use of pembrolizumab among the patients had metastatic triple negative breast cancer and did not receive any treatment yet.

Study Design: Comparative/Observational study.

Place and Duration: Breast Clinic Ganga Ram Hospital Mazang Road, Lahore. April 2021-Sep 2021

Methods: Total 70 patients of aged 25-75 years were presented in this study. Patients had metastatic triple negative breast cancer and did not receive any treatment yet were included. Demographically detailed of enrolled cases age, body mass index, co-morbidities and literacy were calculated after taking informed written consent. Patients were equally divided into two groups, I and II. Group I had 35 patients and received pembrolizumab 200 mg every 2-weeks for six months while in group II 35 patients received chemotherapy (75mg Adriamycin) every 21-days for six months. Regular follow up among patients were conducted. Post-treatment outcomes among both groups were assessed and compared in terms of efficacy, control of disease, mortality and recurrence rate. SPSS 24.0 version was used to analyze complete data.

Results: Mean age of the patients in group I was 58.01±4.34 years with mean BMI 28.21±6.22 kg/m^2 and in group II mean age was 57.88±6.88 years with mean BMI 27.94±9.42 kg/m^2. Frequency of literacy in group I was 18 (51.4%) and in group II 20 (57.1%) patients were literate. Hypertension was the most common comorbidity found in 13 (37.1%) in group I and 14 (40%) in group II followed by arthritis and diabetes mellitus. Post-treatment effectiveness in group I was 15 (42.9%) higher as compared to group II 10 (28.6%), partial recovery found in 11 (31.4%) and 8 (22.9%) among both groups, stability in disease was found higher among patients of group II 12 (34.3%) as compared to group I 7 (20%). Mortality in group I was 3 (8.6%) and in group II 5 (14.3%). Recurrence rate in pembrolizumab group was 2 (5.7%) lower as compared to chemotherapy group 4 (11.4%).

Conclusion: In this research we concluded that the use of pembrolizumab injection for the treatment of breast cancer was effective and useful in terms of low mortality rate with recurrence rate and higher number of recovery, but rate of stability among disease was higher in chemotherapy group. Both treatments were effective for reduction in the prevalence of disease.

Keywords: Breast Cancer, Chemotherapy, Pembrolizumab, Mortality, Recurrence

INTRODUCTION

The absence of oestrogen and progesterone receptor expression and the overexpression or amplification of the human epidermal growth factor receptor-2 gene separate TNBC from other types of breast cancer. There are no effective treatments for triple-negative breast cancer (TNBC), save for BRCA gene-related tumours, due to the lack of targeted therapeutics. [1–3] First-line treatment for patients with metastatic TNBC is cryotoxic chemotherapy (mTNBC). The median overall survival (OS) for patients in this cohort is less than two years after receiving first-line chemotherapy and a RECIST response in about one-third of those individuals. Chemotherapy is often accompanied by a high amount of toxicity in many patients. Metastatic TNBC necessitates the development of novel treatments.[4]

Cancer cells can evade detection by the immune system by using the PD-1 (programmable death receptor 1) pathway [5, 6]. Immune system proteins PD-1 and their receptor ligands, such as PD-L1 and PD-L2, are inhibited when they interact with PEMBOLIZUMAB, a humanised monoclonal antibody of the type IgG4-j subclass that is highly selective. PD-L1 has been found in about half of all breast malignancies, with expression being substantially higher in TNBC than in normal breast tissue [7,8]. Tolerable safety and anticancer efficacy were observed in a group of patients with previously treated PD-L1 metastatic TNBC in the phase Ib KEYNOTE-012 study (N 14 32). These patients had received pembrolizumab therapy for a prolonged period of time. [9]

Charlson Comorbidity Index (CCI) ratings of 1, 2 and >3 suggested that breast cancer survivors with increasing comorbidities had increased likelihood of non-routine disposition, longer hospitalisation and in-patient death when compared to breast cancer survivors with CCI zero. Breast cancer survivors who have comorbidities such as diabetes and high blood pressure are more likely to have unfavourable outcomes after their treatment. The impact of comorbidities on breast cancer survivors' quality of life has been overlooked. I think this is a topic that should be further studied Since breast cancer survival rates and lengths are increasing, quality of life for breast cancer survivors is becoming a more important metric [10,11].

Using self-reported data, researchers have been unable to determine the impact of comorbidities on breast cancer survivors' quality of life. .. Breast cancer survivors' quality of life was studied by Deshpance and colleagues [11] for a year after diagnosis. As established by Katz's comorbidity evaluation, breast cancer survivors with more chronic illnesses had lower physical and social functioning (as assessed by the RAND 36-Item Health Survey). Symptoms of a concomitant illness could only be ascertained by having patients self-report their symptoms in the case of 66% of patients who had no chronic disease burden. In a study of older cancer patients, Smith and colleagues looked at the link between cancer, comorbid conditions, and health-related quality of life (HRQOL) [12]. Breast cancer survivors with two or more comorbidities, especially those diagnosed in the recent year, had a lower quality of life. Prior to and throughout treatment, medically diagnosed comorbidities have a substantial impact on breast cancer survivors' quality of life, as well as the patterns of comorbidity development and their impact on the quality of life of survivors.

The KEYNOTE-086 study enrolled two groups of patients with mTNBC who received pembrolizumab as a monotherapy. A total of 170 previously treated mTNBC patients with PD-L1 expression in Cohort A were enrolled. With pembrolizumab, the ORR was 5.3% and the adverse effects were well-managed in this context; [13]

Patients with untreated PD-L1 positive metastatic triple negative breast cancer will be the focus of our study, which aims to compare the outcomes of chemotherapy with radiology and the usage of pembrolizumab.

MATERIAL AND METHODS

This observational/comparative study was conducted at Breast Clinic Ganga Ram Hospital Queens Road, Lahore and comprised of 70 patients. Demographically detailed of enrolled cases age, body mass index, co-morbidities and literacy were calculated after taking informed written consent. Patients previously received chemotherapy, less than 25 years of age and those did not give any written consent were excluded from this study.

Patients were aged between 25-75 years of age. Patients had metastatic triple negative breast cancer and did not receive any treatment yet were included. In order to validate TNBC status and determine the status of PD-L1, Only newly obtained core or excisional biopsy samples (preferred) or archival tumour tissue from a non-irradiated lesion might be used for central confirmation. Patients were split into two groups, I and II, with equal numbers of patients in each. Group I had 35 patients and received pembrolizumab 200 mg every 2-weeks for six months while in group II 35 patients received chemotherapy (75mg Adriamycin) every 21-days for six months. Disease progression, unacceptable toxicity, medical decision or patient refusal to agree were all factors that led to treatment being halted. Patients who are clinically stable but have radiologic signs of disease progression can continue treatment until the following imaging assessment, three weeks later, confirms radiologic progression. CT or MRI were utilized at the beginning of the study and every six weeks for the first six months, then every four weeks for the rest of the study. The expression of PD-L1 was tested in the laboratory.

Vital signs were monitored on a regular basis throughout the course of the study and at various points during the course of the physical examination and laboratory tests. Post-treatment outcomes among both groups were assessed and compared in terms of efficacy, control of disease, mortality and recurrence rate. SPSS 24.0 version was used to analyze complete data. Mean standard deviation was used. Categorical variables were assessed by frequencies and percentages.

RESULTS

Mean age of the patients in group I was 58.01±4.34 years with mean BMI 28.21±6.22 kg/m^2 and in group II mean age was 57.88±6.88 years with mean BMI 27.94±9.42 kg/m^2. Frequency of literacy in group I was 18 (51.4%) and in group II 20 (57.1%) patients were literate. Hypertension was the most common comorbidity found in 13 (37.1%) in group I and 14 (40%) in group II followed by arthritis, diabetes mellitus, kidney problem, heart disease and thyroid problems.(table 1)

Table 1: Baseline detailed characteristics of presented cases

Variables	G I (35)	G II (35)
Mean age (years)	58.01±4.34	57.88±6.88
Mean BMI (kg/m^2)	28.21±6.22	27.94±9.42
Education status		
Yes	18 (51.4%)	20 (57.1%)
No	17 (47.6%)	15 (42.9%)
Co-morbidities		
Hypertension	13 (37.1%)	14 (40%)
Arthritis	10 (28.6%)	8 (22.9%)
Diabetes mellitus	8 (22.9%)	9 (25.7%)
kidney problem	1 (2.9%)	2 (5.7%)
Heart disease	2 (5.7%)	1 (2.9%)
Thyroid problems	1 (2.9%)	1 (2.9%)

Post-treatment effectiveness in group I was 15 (42.9%) higher as compared to group II 10 (28.6%), partial recovery found in 11 (31.4%) and 8 (22.9%) among both groups, stability in disease was found higher among patients of group II 12 (34.3%) as compared to group I 7 (20%). (table 2)

Table 2: Post-treatment comparison of outcomes among both groups

Variables	Pembrolizumab	Chemotherapy
Outcomes		
Effectiveness	15 (42.9%)	10 (28.6%)
Partial Recovery	11 (31.4%)	8 (22.9%)
Disease Stability	7 (20%)	12 (34.3%)
Total	33 (94.3%)	30 (85.7%)

Table 3: Comparison of mortality and recurrence among both groups

Variables	Pembrolizumab	Chemotherapy
Mortality		
Yes	3 (8.6%)	5 (14.3%)
No	32 (91.4%)	30 (85.7%)
Recurrence		
Yes	2 (5.7%)	4 (11.4%)
No	33 (94.3%)	31 (88.6%)

Mortality in group I was 3 (8.6%) and in group II 5 (14.3%). Recurrence rate in pembrolizumab group was 2 (5.7%) lower as compared to chemotherapy group 4 (11.4%). (table 3)

We found treatment and infusion related adverse outcomes among both groups. Frequency of adverse events in pembrolizumab was significantly lower as compared to chemotherapy group.(table 4)

Table 5: Prevalence of AE's among both groups

Variables	Pembrolizumab	Chemotherapy
Treatment Related AE's		
Fatigue	9 (25.7%)	8 (22.9%)
Nausea	5 (14.3%)	6 (17.1%)
Diarrhea	3 (8.6%)	5 (14.3%)
Anemia	1 (2.9%)	2 (5.7%)
Pruritus	1 (2.9%)	1 (2.9%)
Immune-mediated AEs		
Hypothyroidism	3 (8.6%)	5 (14.3%)
Hyperthyroidism	2 (5.7%)	3 (8.6%)
Pneumonitis	2 (5.7%)	3 (8.6%)
Adrenal insufficiency	1 (2.9%)	2 (5.7%)
Colitis	1 (2.9%)	1 (2.9%)

DISCUSSION

Pembrolizumab monotherapy demonstrated an acceptable safety profile in patients with PD-L1-positive mTNBC who had not previously received treatment for metastatic disease. Pembrolizumab monotherapy exhibited antitumor effectiveness in a small sample of patients with previously treated mTNBC. Despite having a lower ORR than single-agent chemotherapy, Pembrolizumab avoided common chemotherapy effects and provided long-lasting results (5.3 percent). There was a substantial, long-lasting antitumor effect with pembrolizumab as the first line of treatment for patients who were positive for the protein PD-L1.[14]

In this observation/comparative study 70 patients had metastatic triple negative breast cancer and did not receive any treatment yet with ages 25-75 years were presented. Patients were split into two groups, I and II equally. Group I had 35 patients and received pembrolizumab 200 mg every 2-weeks for six months while in group II 35 patients received chemotherapy (75mg Adriamycin) every 21-days for six months. Mean age of the patients in group I was 58.01±4.34 years with mean BMI 28.21±6.22 kg/m^2 and in group II mean age was 57.88±6.88 years with mean BMI 27.94±9.42 kg/m^2. Findings of current research showed resemblance to the previous conducted studies.[14,15] Frequency of literacy in group I was 18 (51.4%) and in group II 20 (57.1%) patients were literate. Hypertension was the most common comorbidity found in 13 (37.1%) in group I and 14 (40%) in group II followed by arthritis and diabetes mellitus. Because the majority of patients have been diagnosed with at least one of the comorbidities, it is important to measure the impact on patients' quality of life. These findings were comparable to the previously conducted studies.[16,17]

In present study, post-treatment effectiveness in group I (pembrolizumab) was 15 (42.9%) higher as compared to group II (chemotherapy) 10 (28.6%), partial recovery found in 11 (31.4%) and 8 (22.9%) among both groups, stability in disease was found higher among patients of group II 12 (34.3%) as compared to group I 7 (20%). Recently study conducted in Pakistan presented same results that injection pembrolizumab was an effective and useful monotherapy among patients with PD-L1-positive mTNBC with less adverse outcomes and higher rate of efficacy.[18] Other studies using immune checkpoint inhibitors for mTNBC treatment have shown similar results. mTNBC was treated with pembrolizumab in the KEYNOTE-012 research, which found an ORR of 18.5%, a median latency to response of 4.1 months, and an unreachable median response duration (between 3.4 and 10.9 months) in the 32 participants.[9] Mortality in group I was 3 (8.6%) and in group II 5 (14.3%). Recurrence rate in pembrolizumab group was 2 (5.7%) lower as compared to chemotherapy group 4 (11.4%). We found treatment and infusion related adverse outcomes among both groups. Frequency of adverse events in pembrolizumab was significantly lower as compared to chemotherapy group. Our findings were comparable to the studies conducted in past.[19,20]

Because of concerns regarding comorbidity and medication toxicity, age has been shown to be an important factor in deciding cancer treatments, particularly chemotherapy.[21,22] The decreased efficacy of chemotherapy for breast cancer with age may have altered oncologists' and patients' knowledge and attitudes about the benefits and hazards of chemotherapy for breast cancer patients as they got older. In women with breast cancer, chemotherapy effectiveness and efficacy decline with age, but not in men and women with colon cancer.[23,24] Patients with previously untreated PD-L1-positive mTNBC were generally well tolerated by pembrolizumab monotherapy, according to our study. Only 15% of patients experienced a grade 3 AE as a result of their treatment. First-line treatment with pembrolizumab monotherapy for patients with PD-L1-positive mTNBC revealed a manageable safety profile and maintained anticancer effectiveness.

CONCLUSION

In this research we concluded that the use of pembrolizumab injection for the treatment of breast cancer was effective and useful in terms of low mortality rate with recurrence rate and higher number of recovery, but rate of stability among disease was higher in chemotherapy group. Both treatments were effective for reduction in the prevalence of disease.

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