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Efficacy and Satisfaction among HER2 Positive Breast Cancer Patients Undergoing Subcutaneous Injection of PHESGO along with Chemotherapy: A Case Series

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Background: The prevalence of Human Epidermal Growth Factor Receptor 2 positive (HER2+) breast cancer (BC) in India ranged from 11% to 17%. A combination of intravenous (IV) pertuzumab, trastuzumab and docetaxel in HER2+ BC reported a significant increase in the overall survival rate. However, the time taken for infusion of these drugs is lengthy. PHESGO, a combination of these two drugs along with hyaluronidase is provided subcutaneously and the time taken is 5-8 minutes. Despite patient preference for PHESGO, its efficacy and satisfaction levels in the Indian context remain unexplored. This case series investigates the efficacy of PHESGO with chemotherapy and assesses the level of satisfaction reported by HER2+ BC patients.

Methods: HER2+ BC patients were identified retrospectively from January 2022 to November 2023. Interviews during follow-ups assessed patient satisfaction. Efficacy was evaluated based on Positron Emission Tomography (PET) scans for metastatic/adjuvant settings and pathological complete response (pCR) rate for neoadjuvant cases.

Results: In total 27 HER2+ BC patients received PHESGO treatment with a median age of 54.5 years. Patients who received PHESGO with chemotherapy in neoadjuvant and metastatic settings were 44.4% and 51.9% respectively. The median cycle of PHESGO with chemotherapy was 5. Neoadjuvant patients showed an 83.3% pCR rate, while 85.7% of metastatic patients reported partial response after three cycles. Among 25 patients, 92% were satisfied with subcutaneous administration of PHESGO.

Conclusion: The findings support the potential of PHESGO as an effective and convenient treatment option for HER2+ BC patients. However, further research, including larger prospective studies and long-term follow-ups, is warranted to comprehensively evaluate the

safety profile, quality of life, and comparative effectiveness of PHESGO versus intravenous administration.

Introduction

In India, the prevalence of Human Epidermal Growth Factor Receptor 2 positive (HER2+) breast cancer ranged from 11% to 17% [1]. It is also associated with high disease recurrence and short survival [2].

The combination of intravenous pertuzumab, trastuzumab, and docetaxel in HER2+ breast cancer reported a significant increase in the overall survival rate in the CLEOPETRA study group [3]. The NeoSphere study conducted by Gianni et al. reported that neoadjuvant intravenous pertuzumab and trastuzumab in women with HER2+ breast cancer significantly improved the pathological complete response (pCR) rate [4]. The adjuvant intravenous pertuzumab and trastuzumab (APHINITY study) significantly improved disease-free survival among early HER2+ breast cancer patients with a high risk of recurrence [5]. Hence, pertuzumab and trastuzumab, along with chemotherapy, are considered the standard care treatment for early and metastatic HER2+ breast cancer patients.

The preparation time for invasive intravenous in medical centers is time-consuming and requires resources to prepare and administer the infusion and dispose of associated materials [6]. Additionally, the time taken for the infusion of pertuzumab is 30-60 minutes and trastuzumab is 30-90 minutes, given multiple cycles over the treatment period. Since intravenous infusions are invasive, they become inconvenient, painful, and time-consuming for patients, especially those who were repeatedly treated. Also, the observation time post-infusion is 2-3 hours [7, 8].

Multiple randomized controlled trials have reported that subcutaneous trastuzumab has similar efficacy, and its safety remains consistent compared to intravenous (IV) trastuzumab in both neoadjuvant and metastatic HER2+ breast cancer [9-14]. Studies also reported that the administration of subcutaneous injection reduces patient spending time, medical resources, and in-patient burden at the medical center, [6] and also preferred by patients [12, 14]. Several benefits were also reported while administering subcutaneous injections, such as improved quality of life, facilitation of home-based therapy, and reduced cost of treatment [15, 16].

The approval of PHESGO, a combination of pertuzumab, trastuzumab and hyaluronidase for subcutaneous injection, by the USFDA in June 2020 and the European Medicine Agency (EMA) in December 2020, along with its recognition in National Comprehensive Cancer Network (NCCN) guidelines, marked a significant milestone [17]. This novel treatment can be administered in a remarkably short time frame of approximately 5-8 minutes, as evidenced by the PHranceSCa and FeDeriCa studies. Notably, these studies found that most patients preferred PHESGO over the traditional intravenous administration of pertuzumab and trastuzumab [18, 19]. Recognizing the potential benefits of PHESGO, it received approval from the DCGI in India in October 2021, and an import license was granted in January 2022. Subsequently, the treatment was administered across India [20]. However, it’s important to note that no study has yet reported on the reasons for patient preference, quality of life, safety, and treatment satisfaction of HER-2+ breast cancer patients in the Indian population who underwent PHESGO treatment.

In light of this knowledge gap, it becomes imperative to assess treatment satisfaction, side effects, and overall efficacy in HER-2+ breast cancer patients who have undergone PHESGO treatment in our setting. Hence, this case series is likely a first-of-its-kind to investigate the efficacy of PHESGO treatment along with chemotherapy and assess the level of satisfaction reported by HER-2+ breast cancer patients.

Methods

All individuals diagnosed with HER-2+ breast cancer and undergoing PHESGO treatment at our institution from January 2022 to November 2023 were retrospectively identified using Electronic Medical Records (EMR). Treatment adhered to established standards of care. Subsequently, patients were contacted during follow-up visits and underwent interviews. Informed consent was obtained from all eligible participants.

The clinical data of the patients, such as the date of diagnosis, information on treatment and surgery, comorbidities, breast cancer subtypes, intent of PHESGO treatment, and the number of cycles of PHESGO received, were extracted from the EMR retrospectively. As per our institutional standards, outcome information, such as Positron Emission Tomography (PET) scan reports and Residual Cancer Burden (RCB) scores to assess the efficacy of PHESGO in metastatic and neoadjuvant treatment settings, was also extracted, respectively. Further, RCB scores were categorized into pCR present or absent.

In the metastatic setting, the response was captured after 3 cycles of PHESGO treatment to assess efficacy. Patient-related satisfaction levels and concerns associated with PHESGO injection were obtained through survey questions adapted from the Rituximab Administration Satisfaction Questionnaire for patients receiving Rituximab subcutaneous (RASQ-SC) (23). A semi-structured interview with probing questions was created based on RASQ-SC. The questionnaire was completed by the patients on the same day. Data were collected on paper and cross-examined by another author to ensure correctness and completeness. The data were then transferred to Excel for further analysis.

Data Analysis

Discreet variables were reported in frequency and percentage. Continuous variables such as age and number of PHESGO cycles were presented as mean and standard deviation (SD) or median and inter-quartile range (IQR). Histogram and Sapiro-Wilk test were used to assess the normality of the continuous variables.

Results

A total of 27 patients with HER2+ breast cancer underwent PHESGO treatment between January 2022 and November 2023 and provided consent to participate. The median age of the patients was 54.5 years, with an interquartile range spanning from 42.8 to 60.3 years. More than half of the patients belonged to the Estrogen Receptor negative (ER-)/progesterone Receptor negative (PR-)/ HER2+ subtypes (59.3%) and had undergone surgery (59.3%). Those who received PHESGO intervention in the neoadjuvant and metastatic settings accounted for 44.4% and 51.9%, respectively. The median number of PHESGO cycles administered to the patients was 5, with an interquartile range ranging from 4 to 6.5 (Table 1).

Characteristics	N (n=27)	%
Age (in Years), (Median, IQR)	54.5 (42.8, 60.3)	
Breast Cancer Subtypes		
ER-/PR-/HER2+	16	59.3
ER+/PR+/HER2+	11	40.7
Surgery		
Yes	16	59.3
No	11	40.7
Co-morbidities		
Yes	9	33.3
No	18	66.7
Clinical setting of PHESGO		

administration		
Neoadjuvant	12	44.4
Adjuvant	1	3.7
Metastatic	14	51.9
Number of PHESGO cycles received (Median, IQR)	5 (4, 6.5)	

Table 1. Demographic and Clinical Characteristics of Breast Cancer Patients.

Outcome in Neoadjuvant, Adjuvant and Metastatic Settings of PHESGO intervention

A total of 12 patients underwent neoadjuvant PHESGO treatment in combination with chemotherapy. Among these patients, the pCR rate was observed in 83.3% (n=10). In the adjuvant setting, one patient achieved disease-free status after completing 8 cycles of PHESGO treatment. In the metastatic setting (n=14), 85.7% (n=12) of the patients reported a partial response after undergoing 3 cycles of PHESGO treatment. However, the comprehensive outcomes in the metastatic setting are detailed in Table 2.

Outcome in Neoadjuvant PHESGO Intervention (n=12)		
Pathological Complete Response (pCR)	N	%
Present	10	83.3
Absent	2	16.7
pCR in Estrogen Receptor (ER) (n=10)		
ER positive	2	20
ER negative	8	80
Outcome in Metastatic patients after 3 cycles of PHESGO (n=14)		
Outcome	N	%
Stable Disease	1	7.1
Partial Response	12	85.7
Disease Progressed	1	7.1
Overall outcome of Metastatic PHESGO Intervention till November 2023 (n=14)		
Stable Disease	5	35.7
Partial Response	7	50
Disease Progressed	2	14.3

Table 2. Outcome in Neoadjuvant, Adjuvant and Metastatic Settings of PHESGO Intervention.

Satisfaction rate among HER2+ breast cancer patients receiving PHESGO intervention subcutaneously

Out of 27 patients, 2 patients died during the study period; hence, the information-related satisfaction rate included 25 patients among which three patients switched from intravenous dual anti-HER2+ drugs to PHESGO. Out of 25 patients, 23 were satisfied with the subcutaneous route administration of the drug. Major reasons for satisfaction were time savings (100%, n=23), less pain and discomfort (65.2%, n=19), and reduced hospital visits (95.6%, n=22). More than half of the patients felt anxious about having a subcutaneous route of injection. The majority of them did not find it convenient to receive the PHESGO injection, citing its expense as stated in Table 3.

Satisfaction Rate	N (n=25)	%
Were you satisfied or dissatisfied with the subcutaneous route of PHESGO		
Satisfied	23	92
Dissatisfied	2	8
Reasons for satisfaction (n=23)		
Time Saving	23	100
Less pain/discomfort/side-effects	19	65.2
Reduced hospital visit	22	95.6
Do you feel anxious about having the subcutaneous injection?		
Yes	14	56
No	11	44
Is it cost-effective to get your PHESGO injection as compared to chemotherapy?		
Yes	8	32
No	17	68
Patients Preference		
Subcutaneous	23	92
Intravenous	2	8

Table 3. Satisfaction Rate among HER2+ Breast Cancer Patient Receiving PHESGO Intervention Subcutaneously.

Discussion

The FeDeriCa and PHranceSCa clinical trials documented the efficacy and safety of the PHESGO intervention within the clinical trial setting [18, 19]. However, none of these studies explored the effectiveness of PHESGO in a real-world context. Consequently, this case series aims to address the efficacy and satisfaction rates among HER-2+ breast cancer patients. All patients with HER-2+ breast cancer who received PHESGO in conjunction with chemotherapy, whether in the neoadjuvant, adjuvant, or metastatic setting, reported favourable outcomes. Therefore, the efficacy of the PHESGO subcutaneous route of administration, along with chemotherapy, aligns with the results from the FeDeriCa and PHranceSCa clinical trials [18, 19].

The satisfaction rate regarding PHESGO subcutaneous intervention was reported to be higher in our case series. Similar findings were reported by Dent et al. [21], although the subcutaneously administered drug in their study was trastuzumab. Reasons for satisfaction with the subcutaneous route of administration included time-saving and reduced pain and discomfort, which are consistent with the findings reported by Jackisch et al. [22] This case series has several strengths. To the best of our knowledge, this is the first case series in India that focused on assessing the efficacy and satisfaction rate among HER2+ breast cancer patients receiving PHESGO along with chemotherapy. Along with the satisfaction rate, we also collected information on convenience and preference associated with receiving the subcutaneous route of PHESGO. This study also contributes to the body of real-world evidence.

However, it is essential to acknowledge the many limitations in our study. A limited number of cases and short follow-ups restrict the generalizability of the findings. Notably, we did not conduct a comparative analysis of patient satisfaction rates between the intravenous and subcutaneous routes, a comparison that could have offered a clearer understanding of the preferences for either route of administration. Additionally, we omitted the collection of information regarding potential side effects experienced by patients during PHESGO treatment. This aspect could have been addressed through a more comprehensive follow-up assessment, offering a more thorough exploration of the patient experience and treatment outcomes.

The findings from this case series encourage and inform future studies aimed at identifying whether PHESGO subcutaneous is satisfactory as compared to the intravenous route. Also, larger prospective studies and follow-up studies will provide the side-effects and quality of life of the patients which can be associated with the route of administration. Although PHESGO is reported to be effective, cost plays a major role concerning access injection. Hence, cost-effectiveness studies can help in providing policy change and increase convenience in accessing PHESGO treatment.

Consent

All the patients provided written informed consent to report their case, including clinical, demographic, and satisfaction information within this case series.

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Nil

Conflict of Interest

There are no conflicts of interest.

Ethical Approval

Ethical approval for this case series was obtained from the Biomedical and Health Research Committee For Sahyadri Hospitals.

Authors Contribution

Dr Shona Nag (SN), Dr Anupama Mane (AP), Abhilash Patra (AP): Conceptualization, Investigation, Visualization, Writing – Original Draft; Dr Madhuri Dhobale (AD), Kavitha Varghese (KV): Resources, Data Extraction and management; Dr Varun Agiwal (VA), Hira B Pant (HBP), Dr Nirupama A Y (NAY), AP: Project Administration, Writing – Review and Editing; Dr G V S Murthy, SN, AP: Supervision, Writing – Review and Editing, and all authors approved the manuscript.

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