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Original Article

Polymeric Nanoparticles for Targeted Chemotherapy in Breast Cancer Patients

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ABSTRACT

Background: Polymeric nanoparticles are being investigated as drug-delivery systems for breast cancer because of their potential to modify drug release and distribution, although clinical evidence remains limited. Objective: To evaluate tumor response, treatment-emergent adverse effects, and short-term clinical outcomes among breast cancer patients receiving PLGA-based polymeric nanoparticle chemotherapy. Methods: A prospective observational pilot study included 40 women with stage II or III breast cancer treated at selected oncology centers in Khyber Pakhtunkhwa, Pakistan. Tumor response was assessed clinically and radiologically, adverse events were documented during treatment, and vital status was recorded during follow-up. Descriptive statistics and 95% confidence intervals were used to summarize outcomes. Results: Mean age was 49.6 ± 9.8 years. Complete response occurred in 5 patients (12.5%) and partial response in 24 (60.0%), producing an objective response rate of 72.5% (95% CI 57.2–83.9). Disease control was observed in 92.5% (95% CI 80.1–97.4). Tumor-size reduction of ≥25% occurred in 72.5% of patients. Mild nausea/vomiting occurred in 35.0%, fatigue in 32.5%, neutropenia in 17.5%, severe anemia in 7.5%, and toxicity-related hospitalization in 5.0%. At the end of documented follow-up, 36 patients were alive and four had died from disease-related causes. Conclusion: The cohort demonstrated measurable tumor responses and a clinically describable tolerability profile following nanoparticle-based chemotherapy; however, the uncontrolled pilot design does not establish comparative effectiveness, reduced toxicity, direct tumor-targeting efficiency, or long-term survival benefit. Keywords: Breast cancer; polymeric nanoparticles; targeted chemotherapy; nanomedicine; PLGA nanoparticles; drug delivery; chemotherapy toxicity; precision oncology.

INTRODUCTION

Breast cancer remains one of the most frequently diagnosed malignancies among women and continues to contribute substantially to cancer-related morbidity and mortality worldwide. Despite advances in screening, surgical management, radiotherapy, endocrine therapy, molecularly targeted treatment, and systemic chemotherapy, treatment failure and therapy-related adverse effects remain important clinical challenges. Chemotherapy continues to play a central role in the management of locally advanced and biologically aggressive breast cancer; however, conventional cytotoxic agents generally have limited selectivity for malignant tissue and may expose normal organs to pharmacologically active drug concentrations. Consequently, treatment can be accompanied by gastrointestinal symptoms, fatigue, alopecia, myelosuppression, infection, hematological abnormalities, and other toxicities that can adversely affect treatment tolerance and continuity (1,2).

Nanotechnology-based drug-delivery systems have been developed to improve the pharmacological characteristics of anticancer agents by modifying their distribution, stability, solubility, release profile, and interaction with tumor tissues. Among the available nanocarrier platforms, polymeric nanoparticles have received considerable attention because biodegradable polymers can encapsulate or associate with chemotherapeutic drugs and permit controlled drug release while protecting incorporated agents from premature degradation. Commonly investigated polymeric systems include poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol-containing systems, chitosan-based carriers, and other biodegradable polymers. These materials have been investigated for their potential to enhance drug delivery while limiting unnecessary systemic exposure (3–6).

The biological rationale for nanoparticle-assisted cancer therapy includes differences between malignant and normal tissue microenvironments. Many solid tumors demonstrate abnormal vascular architecture, heterogeneous perfusion, increased vascular permeability, and impaired lymphatic drainage, characteristics that may permit some nanoparticle formulations to accumulate within tumor tissue through mechanisms commonly associated with the enhanced permeability and retention effect. Nevertheless, nanoparticle deposition within human tumors is heterogeneous and depends on several interacting factors, including particle size, surface properties, polymer composition, circulation characteristics, tumor vascularity, and the surrounding microenvironment. In addition to passive accumulation, polymeric nanoparticles can be modified with ligands, peptides, antibodies, folate derivatives, or receptor-directed molecules to promote interaction with selected cellular targets. These approaches are intended to improve drug delivery rather than guarantee selective tumor localization in every patient (10–13).

PLGA-based nanoparticles are particularly relevant to anticancer drug delivery because PLGA is biodegradable and has been extensively investigated as a carrier for controlled and sustained release of therapeutic compounds. Experimental studies involving doxorubicin, docetaxel, cisplatin, and other anticancer agents have shown that polymeric nanoparticle formulations can alter intracellular drug delivery and improve antitumor activity in preclinical breast cancer models (14–20). Studies involving taxane-resistant and multidrug-resistant breast cancer models have also suggested that nanoparticle-mediated delivery may increase intracellular exposure to chemotherapeutic agents and modify mechanisms contributing to treatment resistance (15,16,18). These findings provide a biological rationale for clinical evaluation; however, results from laboratory and animal studies cannot be assumed to translate directly into superior clinical effectiveness or reduced toxicity in patients.

The potential importance of improved drug-delivery strategies is further emphasized by the biological heterogeneity of breast cancer. Breast tumors include hormone receptor-positive, HER2-positive, and triple-negative phenotypes that differ in prognosis, therapeutic responsiveness, recurrence risk, and available targeted treatments. Triple-negative breast cancer remains particularly challenging because of its aggressive clinical behavior and comparatively limited range of receptor-directed therapeutic options. Polymeric nanoparticle platforms have therefore been investigated not only as carriers for conventional cytotoxic agents but also as potential systems for improving intracellular drug delivery in resistant and difficult-to-treat breast cancer models (14–18).

Breast cancer also represents an important healthcare burden in Pakistan, where patients may encounter delayed presentation and unequal access to specialized diagnostic and oncology services. Such challenges are particularly relevant when evaluating treatment approaches intended to improve therapeutic tolerability and optimize delivery of anticancer agents. At the same time, advanced nanomedicine-based treatments require careful assessment of manufacturing quality, clinical feasibility, treatment safety, cost, and reproducibility before they can be incorporated into routine oncology practice. Clinical evidence from Pakistani populations concerning polymeric nanoparticle-based chemotherapy remains limited, particularly regarding tumor response, treatment-emergent adverse effects, and short-term clinical outcomes.

Most available evidence supporting polymeric nanoparticle systems in breast cancer originates from formulation studies, experimental models, and preclinical investigations, whereas comparatively fewer clinical data are available describing outcomes among patients receiving such formulations. Furthermore, clinical tumor response cannot itself be considered a direct measurement of nanoparticle biodistribution or tumor-specific accumulation. Evaluation in patients should therefore distinguish measurable clinical outcomes, such as changes in tumor burden, objective response categories, adverse-event frequencies, and survival status, from mechanistic claims concerning nanoparticle localization that require dedicated pharmacokinetic, biodistribution, or molecular imaging investigations.

Accordingly, the present prospective clinical pilot study evaluated clinical outcomes among breast cancer patients receiving PLGA-based polymeric nanoparticle chemotherapy in oncology centers in Khyber Pakhtunkhwa, Pakistan. The primary objective was to characterize tumor response following nanoparticle-based chemotherapy using clinical and imaging assessments. The secondary objectives were to describe treatment-related adverse effects and evaluate short-term clinical outcomes, including progression and survival status during follow-up. The study was intended to provide preliminary clinical evidence regarding the response and tolerability profile of polymeric nanoparticle-based chemotherapy and to inform the design of larger controlled investigations assessing comparative effectiveness, safety, and clinically meaningful tumor-targeting properties.

MATERIALS AND METHODS

A prospective observational pilot study was conducted among patients with histopathologically confirmed breast cancer receiving polymeric nanoparticle-based chemotherapy at selected oncology centers in Khyber Pakhtunkhwa, Pakistan. The study was designed to prospectively document clinical response, treatment-emergent adverse effects, and short-term clinical outcomes during and following nanoparticle-based chemotherapy. Because the study did not include a parallel conventional-chemotherapy control group, outcomes were evaluated descriptively within the treated cohort rather than as comparative estimates of superiority over conventional chemotherapy.

The study population consisted of adult female patients aged 18 years or older with breast cancer confirmed through clinical assessment, diagnostic imaging, and histopathological examination who were scheduled to receive chemotherapy as part of their oncology management. Patients with stage II or stage III breast cancer represented the enrolled cohort. Eligibility required a confirmed diagnosis of breast cancer and suitability for chemotherapy according to the treating oncology team. Patients who had previously completed chemotherapy cycles without nanoparticle-based treatment, women who were pregnant, patients with severe uncontrolled medical conditions that could interfere with treatment or follow-up, and individuals who declined participation were excluded. Clinical information was obtained from medical records and direct patient assessment and included age, disease stage, histological characteristics, molecular subtype, previous surgical treatment, treatment history, and relevant clinical status.

A total of 40 eligible patients were included in the pilot cohort. The sample represented patients enrolled during the study recruitment process who met the eligibility requirements and received the nanoparticle-based chemotherapy approach evaluated in the study. Given the exploratory pilot design, the cohort was used to characterize feasibility, clinical response patterns, treatment tolerance, and short-term outcomes and to generate preliminary estimates that could inform subsequent larger controlled studies.

The polymeric drug-delivery system used in the study was based on poly(lactic-co-glycolic acid), a biodegradable polymer widely investigated for controlled drug delivery. The nanoparticle formulation was prepared using an emulsion-based method. The chemotherapeutic agent was incorporated into a polymer-containing phase and subsequently introduced into an aqueous stabilizing phase under continuous mixing to generate a nanoparticle suspension. The preparation process was continued until

a relatively uniform nanoparticle dispersion with stable drug incorporation was obtained. The prepared formulation underwent laboratory characterization of key physicochemical parameters, including particle size, surface charge, drug-loading characteristics, and encapsulation efficiency. Stability and sterility were assessed through the laboratory quality-control procedures applied before clinical administration.

Nanoparticle-based chemotherapy was subsequently administered according to the chemotherapy protocol and dosing decisions established by the treating oncologist for each patient. Clinical treatment decisions remained under the responsibility of the oncology team and were based on the patient's breast cancer characteristics and clinical status. Patients underwent routine clinical monitoring during their chemotherapy cycles, and treatment-related clinical information was prospectively documented throughout the observation period.

The principal clinical outcome was tumor response following nanoparticle-based chemotherapy. Baseline tumor measurements obtained before treatment were compared with findings from subsequent clinical and radiological evaluations. Imaging was performed using computed tomography, magnetic resonance imaging, or another clinically indicated imaging modality according to the requirements of the treating oncology service. Tumor burden was evaluated by comparing pretreatment and post-treatment measurements, and clinical response was categorized as complete response, partial response, stable disease, or progressive disease according to the response assessments recorded during follow-up. Changes in measured tumor size were additionally examined to characterize the magnitude of tumor reduction after treatment.

Tumor response was treated as a clinical efficacy outcome and was not interpreted as a direct measurement of nanoparticle biodistribution or tumor-specific nanoparticle accumulation. Direct tumor-targeting efficiency would require dedicated pharmacokinetic, biodistribution, tissue-concentration, or molecular imaging measurements, which were outside the clinical outcome assessment described in this pilot investigation. The present analysis therefore focused on measurable changes in tumor burden and response status following treatment.

Treatment safety and tolerability were evaluated throughout chemotherapy. Patients were assessed during treatment cycles and follow-up visits for commonly encountered chemotherapy-associated adverse effects, including nausea, vomiting, fatigue, alopecia, neutropenia, anemia, infection-related complications, and other clinically relevant symptoms. Clinical interviews, examination findings, laboratory investigations, and hospital records were used to document adverse events and their clinical severity. Complete blood count and relevant biochemical investigations were performed at clinically indicated intervals to monitor hematological and systemic treatment tolerance. Hospital admissions attributable to treatment-related toxicity were also recorded.

Because the study did not include a concurrent conventional-chemotherapy comparison group, frequencies of adverse events were summarized as treatment-emergent toxicity within the nanoparticle-treated cohort. The observed adverse-event rates were not used to establish a causal reduction in toxicity relative to conventional chemotherapy. This distinction was maintained when interpreting tolerability findings.

Patients were followed during treatment and subsequent clinical visits to document tumor response, evidence of disease progression or recurrence, and vital status. Overall survival was defined from initiation of nanoparticle-based chemotherapy until death from any cause or the last available follow-up. Progression-free survival was defined from treatment initiation until documented disease progression, recurrence, death, or the relevant censoring point according to the available follow-up information. Follow-up data were obtained from clinical examinations, oncology records, radiological reports, and direct patient communication when required.

Data were entered into a structured database and checked for consistency before statistical analysis. Continuous variables were summarized using mean and standard deviation when appropriate, while categorical variables were presented as frequencies and percentages. Demographic and clinical characteristics, molecular subtype distribution, disease stage, treatment response, tumor-size reduction categories, adverse events, hospitalization due to toxicity, and survival status were summarized descriptively. Pretreatment and post-treatment tumor measurements were compared using an appropriate paired statistical approach according to the distribution and completeness of the available measurements. Associations between categorical clinical characteristics and treatment outcomes were evaluated using appropriate contingency-table methods where sufficient observations were available.

Time-to-event outcomes were evaluated using Kaplan–Meier methodology where the available follow-up information permitted estimation of survival functions. Patients without the event of interest at the end of their documented follow-up were treated as censored observations. Statistical significance was assessed using a two-sided threshold of $p<0.05$. Analyses were restricted to observed study data, and no participant-level values were reconstructed or imputed from aggregate results.

The study was conducted in accordance with ethical principles governing research involving human participants. The study protocol underwent institutional ethical review before patient enrollment. All participants were informed about the study purpose, clinical procedures, anticipated benefits, potential risks, confidentiality of their information, and voluntary nature of participation. Written informed consent was obtained before enrollment, and clinical information collected for research purposes was handled confidentially throughout the study.

RESULTS

A total of 40 women with breast cancer were included in the prospective pilot cohort. The mean age was 49.6 ± 9.8 years, corresponding to a 95% confidence interval of 46.5–52.7 years, and 24 participants (60.0%) were aged 40–60 years. Stage III disease was reported in 23 patients (57.5%), while 17 (42.5%) had stage II disease. Invasive ductal carcinoma was the predominant histological diagnosis, occurring in 32 patients (80.0%). According to the molecular subtype categories reported in the study, 18 patients (45.0%) had hormone receptor-positive tumors, 9 (22.5%) had HER2-positive disease, and 13 (32.5%) had triple-negative breast cancer. Previous surgical treatment before chemotherapy was reported in 29 participants (72.5%) (Table 1).

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

Characteristic	n (%) or Mean ± SD	95% CI
Total participants	40	—
Age, years	49.6 ± 9.8	46.5–52.7
Age group, years		
<40	8 (20.0)	—
40–60	24 (60.0)	—
>60	8 (20.0)	—
Disease stage		
Stage II	17 (42.5)	—
Stage III	23 (57.5)	—
Histological type		
Invasive ductal carcinoma	32 (80.0)	—
Other histological types	8 (20.0)	—
Reported molecular subtype		
Hormone receptor-positive	18 (45.0)	—
HER2-positive	9 (22.5)	—
Triple-negative breast cancer	13 (32.5)	—
Previous surgery before chemotherapy		
Yes	29 (72.5)	—
No	11 (27.5)	—

Data are presented as n (%) unless otherwise indicated. The 95% confidence interval for mean age was calculated from the reported mean, standard deviation, and sample size using the t distribution. Molecular subtype categories are reproduced according to the classification reported in the source manuscript.

Table 2. Tumor Response and Magnitude of Tumor-Size Reduction Following Nanoparticle-Based Chemotherapy

Outcome	n (%)	95% CI
Tumor response		
Complete response	5 (12.5)	5.5–26.1
Partial response	24 (60.0)	44.6–73.7
Stable disease	8 (20.0)	10.5–34.8
Progressive disease	3 (7.5)	2.6–19.9
Objective response, complete + partial response	29 (72.5)	57.2–83.9
Disease control, complete + partial + stable disease	37 (92.5)	80.1–97.4
Tumor-size reduction category		
≥50% reduction	18 (45.0)	30.7–60.2
25–49% reduction	11 (27.5)	16.1–42.8
<25% reduction	8 (20.0)	10.5–34.8
No reduction	3 (7.5)	2.6–19.9
≥25% reduction	29 (72.5)	57.2–83.9
Any reported reduction	37 (92.5)	80.1–97.4

CI, confidence interval. Percentage confidence intervals were calculated using the Wilson method from the reported numerator and denominator (n=40). Objective response rate and disease-control rate were derived directly from the mutually exclusive response categories. Aggregate tumor-reduction categories were derived directly from the mutually exclusive reduction categories. Tumor response and tumor-size reduction should not be interpreted as direct measures of nanoparticle biodistribution or tumor-specific nanoparticle accumulation.

Table 3. Treatment-Emergent Adverse Events and End-of-Follow-Up Vital Status

Outcome	n (%)	95% CI
Treatment-emergent adverse events		
Mild nausea/vomiting	14 (35.0)	22.1–50.5
Severe nausea/vomiting	4 (10.0)	4.0–23.1
Fatigue	13 (32.5)	20.1–48.0
Neutropenia	7 (17.5)	8.7–32.0
Severe anemia	3 (7.5)	2.6–19.9
Hospital admission due to toxicity	2 (5.0)	1.4–16.5
Vital status at end of documented follow-up		
Alive	36 (90.0)	76.9–96.0
Disease-related death	4 (10.0)	4.0–23.1

CI, confidence interval. Adverse-event categories were not reported as mutually exclusive; therefore, percentages should not be summed. Confidence intervals were calculated using the Wilson method from n=40. Vital-status percentages describe the status recorded at the end of the available follow-up and do not represent fixed-time survival probabilities because the duration of follow-up was not reported.

Following nanoparticle-based chemotherapy, complete tumor response was observed in 5 patients (12.5%; 95% CI 5.5–26.1), partial response in 24 (60.0%; 95% CI 44.6–73.7), stable disease in 8 (20.0%; 95% CI 10.5–34.8), and progressive disease in 3 (7.5%; 95% CI 2.6–19.9). Consequently, the derived objective response rate, defined as complete or partial response, was 72.5% (29/40; 95% CI 57.2–83.9), while disease control comprising complete response, partial response, or stable disease was observed in 92.5% of participants (37/40; 95% CI 80.1–97.4). These measures describe the clinical response observed in the treated cohort and do not constitute comparative estimates against conventional chemotherapy (Table 2).

Analysis of the reported tumor-size reduction categories showed that 18 patients (45.0%; 95% CI 30.7–60.2) experienced a reduction of at least 50%, while 11 (27.5%; 95% CI 16.1–42.8) demonstrated a

reduction of 25–49%. A reduction of less than 25% was recorded in 8 patients (20.0%; 95% CI 10.5–34.8), and 3 patients (7.5%; 95% CI 2.6–19.9) had no reported reduction. On aggregation of these categories, 29 patients (72.5%; 95% CI 57.2–83.9) demonstrated a tumor-size reduction of at least 25%, while some degree of reduction was reported in 37 patients (92.5%; 95% CI 80.1–97.4). These tumor-size findings represent clinical and radiological treatment outcomes and should not be interpreted as direct evidence of nanoparticle localization or tumor-targeting efficiency.

Treatment-emergent adverse events were documented throughout the observation period. Mild nausea or vomiting was reported in 14 patients (35.0%; 95% CI 22.1–50.5), while severe nausea or vomiting occurred in 4 (10.0%; 95% CI 4.0–23.1). Fatigue was recorded in 13 patients (32.5%; 95% CI 20.1–48.0), neutropenia in 7 (17.5%; 95% CI 8.7–32.0), and severe anemia in 3 (7.5%; 95% CI 2.6–19.9). Two patients (5.0%; 95% CI 1.4–16.5) required hospital admission because of treatment-related toxicity. Because individual patients could experience more than one adverse event and no concurrent conventional-chemotherapy group was included, these findings describe the observed toxicity profile of the nanoparticle-treated cohort rather than demonstrating a reduction in toxicity relative to another treatment strategy (Table 3).

At the end of the documented follow-up, 36 patients (90.0%; 95% CI 76.9–96.0) were alive and 4 (10.0%; 95% CI 4.0–23.1) had experienced disease-related mortality. These observations represent end-of-follow-up vital status only. A fixed-time overall survival probability, median overall survival, progression-free survival estimate, or Kaplan–Meier survival curve could not be reported from the available aggregate results because individual follow-up durations, progression times, event times, and censoring information were not provided.

DISCUSSION

The present prospective observational pilot study evaluated clinical response, treatment-emergent adverse events, and short-term clinical outcomes among 40 women with stage II or III breast cancer receiving PLGA-based polymeric nanoparticle chemotherapy. Complete or partial response was observed in 29 patients, corresponding to an objective response rate of 72.5%, while 37 patients achieved complete response, partial response, or stable disease, yielding a disease-control rate of 92.5%. A reduction in tumor size of at least 25% was reported in 72.5% of the cohort, and some degree of tumor-size reduction was observed in 92.5%. Treatment-emergent adverse events were predominantly gastrointestinal, constitutional, and hematological, while toxicity-related hospitalization occurred in 5.0% of patients. These findings provide preliminary descriptive evidence concerning clinical response and tolerability in this treated cohort but, in the absence of a concurrent comparator, do not establish superiority over conventional chemotherapy or directly demonstrate nanoparticle-specific tumor targeting.

The observed tumor responses are biologically compatible with the pharmacological rationale underlying polymeric nanoparticle drug-delivery systems. PLGA and related biodegradable polymers can encapsulate anticancer agents, protect incorporated drugs from premature degradation, and provide controlled release that may alter drug exposure and cellular uptake (3–6). Nanocarriers have also been investigated as platforms for modifying pharmacokinetics and improving the therapeutic index of anticancer agents (7,8). However, the clinical response observed in the present study should be distinguished from direct measurement of nanoparticle deposition within tumor tissue. Nanoparticle accumulation in solid tumors depends on multiple biological and physicochemical factors, including vascular permeability, interstitial pressure, particle size, surface characteristics, circulation time, polymer composition, and tumor microenvironment heterogeneity (9,10). Consequently, tumor shrinkage provides evidence of treatment response but cannot independently establish the extent of tumor-specific nanoparticle accumulation.

Experimental breast cancer studies provide supportive mechanistic evidence for nanoparticle-mediated delivery of cytotoxic agents. Docetaxel-containing PLGA formulations have demonstrated enhanced

antitumor activity in preclinical models, including taxane-resistant triple-negative breast cancer, while intracellularly targeted polymeric systems have shown potential to overcome mechanisms associated with chemotherapeutic resistance (11–13). Nanoparticle-based co-delivery systems involving doxorubicin, disulfiram, metformin, and other agents have similarly been investigated as approaches to improve intracellular drug exposure and address multidrug resistance (14,15). Targeted nanoparticle systems incorporating receptor-directed ligands have also demonstrated antitumor activity in experimental breast cancer models (16,17). These studies provide a plausible biological framework for the responses observed in the current cohort, although differences in formulation, drug payload, tumor model, dose, and treatment setting prevent direct comparison between preclinical findings and clinical outcomes.

The clinical interpretation of nanoparticle therapy is particularly relevant in biologically heterogeneous breast cancer. The present cohort included hormone receptor-positive, HER2-positive, and triple-negative tumors, with triple-negative disease accounting for 32.5% of patients. Polymeric nanoparticles have been reviewed extensively as potential drug-delivery systems across different breast cancer phenotypes because their physicochemical properties can be adapted to accommodate diverse drug molecules and targeting strategies (18). Nanomaterials are also increasingly being investigated at the interface of diagnostic imaging and cancer therapy, potentially enabling more sophisticated characterization and monitoring of therapeutic delivery (19). Recent literature continues to emphasize the potential of polymeric nanoparticles for targeted drug delivery in breast cancer, although translation into routine clinical practice requires substantially more human evidence than is currently available (20).

Tumor-size reduction was common in the present cohort, with 45.0% of patients demonstrating a reduction of at least 50% and a further 27.5% demonstrating a reduction between 25% and 49%. Nevertheless, tumor-size categories and conventional response categories should not be considered interchangeable without explicit specification of the response assessment criteria and timing of imaging. Future clinical studies should use a predefined validated response framework and standardized imaging intervals so that objective response estimates can be reproduced and compared reliably across studies. This is particularly important for pilot investigations in which small differences in classification can substantially influence response percentages because of the limited sample size.

The adverse-event findings also require cautious interpretation. Mild nausea or vomiting occurred in 35.0% of patients, severe nausea or vomiting in 10.0%, fatigue in 32.5%, neutropenia in 17.5%, and severe anemia in 7.5%, while 5.0% required hospitalization because of treatment-related toxicity. These frequencies describe treatment-emergent toxicity within the nanoparticle-treated cohort but cannot establish that polymeric nanoparticle delivery reduced toxicity relative to conventional chemotherapy. The potential for polymeric nanoparticles to alter systemic drug exposure and controlled release has been extensively discussed in the nanomedicine literature (4–6), and a range of formulation strategies have been developed to improve tumor-directed delivery. These include pH-responsive folate-targeted polymer-coated nanoparticles, PEGylated PLGA systems, magnetic chitosan nanoparticles, and combination-drug polymeric carriers (21–25). Nevertheless, whether such formulations translate into clinically meaningful reductions in adverse events must be determined through direct comparative clinical studies using standardized toxicity grading.

At the end of the documented follow-up period, 36 patients were alive and four had experienced disease-related mortality. These data should be interpreted as vital status at the end of available observation rather than as a formal survival probability. Although the study protocol contemplated time-to-event assessment, meaningful Kaplan–Meier estimates require individual event times, censoring information, and a defined duration of follow-up. In the absence of these data, the present study cannot establish median overall survival, progression-free survival, or fixed-time survival probabilities. Future investigations should prospectively define follow-up intervals, progression criteria, censoring rules, and clinically meaningful survival endpoints.

The study has several strengths. It provides preliminary clinical observations from a Pakistani breast cancer population, includes patients with multiple molecular phenotypes, reports mutually exclusive tumor-response categories, and documents clinically relevant treatment-emergent adverse events. The study also addresses a field in which much of the available evidence remains experimental or preclinical. Nevertheless, its limitations substantially constrain inference. The sample size was small, no concurrent conventional-chemotherapy control group was included, and the duration of follow-up was not adequately specified. The available report did not provide complete quantitative nanoparticle characterization, detailed chemotherapeutic drug and dosing information, standardized toxicity grading, or sufficiently detailed response-assessment procedures. Potential confounding by disease stage, molecular subtype, previous surgery, prior therapy, and other clinical characteristics could not be addressed using the reported aggregate data. Direct pharmacokinetic, biodistribution, tissue-concentration, or molecular-imaging assessments of nanoparticle localization were also not performed; consequently, the study cannot determine tumor-targeting efficiency directly.

These limitations are especially important when considering implementation in routine oncology practice. Nanoparticle formulations require reproducible manufacturing, physicochemical characterization, sterility assurance, stability assessment, regulatory oversight, and evaluation of cost and accessibility in addition to demonstration of clinical efficacy and safety. Larger prospective controlled studies should therefore characterize the nanoparticle formulation and chemotherapy regimen in detail, use standardized tumor-response and toxicity criteria, prespecify clinically meaningful endpoints, and incorporate adequate follow-up for progression and survival analyses. Where the purpose is specifically to establish tumor-targeting efficiency, clinical outcome assessment should be supplemented by appropriate pharmacokinetic, biodistribution, molecular-imaging, or tissue-level measurements.

Overall, the findings should be regarded as preliminary evidence of clinical response and treatment tolerability among patients who received PLGA-based polymeric nanoparticle chemotherapy rather than proof of comparative effectiveness. The relatively high proportions of patients with objective response and disease control justify further clinical investigation, but confirmation will require adequately powered comparative studies capable of separating treatment effects from patient selection, disease biology, concomitant treatment, and other potential confounding factors.

CONCLUSION

Among 40 women with stage II or III breast cancer receiving PLGA-based polymeric nanoparticle chemotherapy, 72.5% achieved a complete or partial tumor response and 92.5% achieved disease control, while treatment-emergent gastrointestinal, constitutional, and hematological adverse events were observed at varying frequencies and 5.0% required toxicity-related hospitalization. These findings indicate measurable clinical response and an assessable tolerability profile within the treated cohort; however, the absence of a concurrent control group, direct nanoparticle biodistribution measurements, and adequately documented time-to-event follow-up prevents conclusions regarding superiority over conventional chemotherapy, reduced toxicity, tumor-targeting efficiency, or long-term survival benefit.

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