ejpmr, 2025, 12(10), 394-407

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN (O): 2394-3211

ISSN (P): 3051-2573

PACLITAXEL-BASED NANOPARTICLE DELIVERY SYSTEMS FOR BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Article Received on 28/08/2025 **Article Revised on 17/09/2025** **Article Accepted on 08/10/2025**

ABSTRACT

Breast cancer is most prevalent among women throughout the world and is a major cause of cancer related mortality. Systemic therapy is incomplete without paclitaxel, which on the one hand has weakly soluble forms (sb-PTX): low solubility limits its applications, and toxicity is not ideal. To overcome these limitations, nanoparticle albumin-bound paclitaxel (nab-PTX) was formulated as more soluble and improved drug delivery system and it eliminates the need for Cremophor EL, the solvent responsible for most hypersensitivity reactions. The comparative efficacy and safety of nab-PTX and sb-PTX is also clinically important, and to support creating an effective treatment regimen. **Objective**: To assess the efficacy and safety of nab-PTX versus sb-PTX in various breast cancer populations such as early-stage, HER2-positive breast cancer and breast cancer metastases. **Data Sources**: PubMed, Elsevier, Springer, Google Scholar, and Research Gate were systematically searched to retrieve English language articles and published from January 2010 to March 2025. **Study Selection:** Eligible studies were randomized controlled trials, prospective or retrospective cohort studies and systematic reviews with meta-analyses comparing nab-PTX with sb-PTX in breast cancer patients directly. Review articles, editorials, case reports and conference abstracts were excluded. **Extract and Data synthesis :**Data Study level data were screened and extracted by two independent reviewers Outcomes included pathological complete response (pCR), objective response rate (ORR) and adverse events. Pooled relative risks (RRs) and odds ratios (ORs) were computed using random effects models. This review was performed according to PRISMA 2020 guidelines. **Main Outcomes and Measures: Primary outcomes**: pCR and ORR. **Secondary outcomes**: Adverse events resulting during treatment such as hypersensitivity, neuropathy, hematological toxicity, gastrointestinal toxicity, alopecia, and fatigue. **Results:** Eight thousand five hundred forty three patients were included in 6 studies. Nab-PTX was more effective with pooled pCR standing at 48.7% compared with 38.2% as compared with sb-PTX (RR, 1.18 [95% CI, 1.081.29]; P <.001). Nab-PTX had an increased ORR (58.7% vs 45.2%; RR, 1.30 [95% CI, 1.07157]; P = .007). Lack of Cremophor EL significantly reduced hypersensitivity reaction with nab-PTX. Peripheral neuropathy had been more common, but was mild and reversible. Nab-PTX demonstrated similar or lower rates of toxicities compared to sb-PTX, particularly with related to hematological and gastrointestinal adverse events. **Conclusions:** Nab-PTX is linked to superior efficacy and better safety profile than sb-PTX in the treatment of breast cancer. These results support nab-PTX as an important therapeutic option especially in patients who are at risk of hypersensitivity reactions or in whom extensive neo adjuvant therapy is required. Long-term survival outcomes, cost-effectiveness and scalability remain areas for further research.

1. INTRODUCTION

Breast cancer is the most common cancer in the world for women and remains the most frequent cause of cancer-related death which will likely reach high numbers as in the US alone the incidence rate will rise to 364,000 by 2040 just in the US.[1] Worldwide, there were approximately 2.3 million new cases in addition to 670,000 deaths from breast cancer in 2022 with a global 5-year survival rate for women with cancer at approximately 85% and observed incidence rate of 94 per 100,000 person-years in the United Kingdom compared to 1.2 per 100,000 for men.[2-4]

Epidemiological research indicates that risk factors associated with HNCR can be also modified, that is alcohol use, obesity, short duration of women breastfeeding, which would led to reduction of the disease burden.[5] Standard treatments currently include surgery, chemo- and/or radio-therapy, with surgery followed by radiotherapy being the standard for early

disease stage but in metastatic stage surgery is primarily palliative. Radiotherapy contributes to prevent recurrence and chemotherapy remains the basis of systemic therapy with alkylating agents, mainly including alkylating agents**.** such as cyclophosphamide.[6,7]

The most useful among them is a taxane derivative, paclitaxel (PTX) that works by stabilizing microtubules, preventing chromosome separation, disrupting mitotic spindle function, and leading to mitotic arrest and finally resulting in apoptosis due to abnormal tubulin assembly.[8] Its effectiveness has been identified through clinical trials, a single phase II study which showed a response rate of 38% and a median progression-free survival of five months in anthracycline-pretreated metastatic patients receiving 175-225 mg/m^2 of paclitaxel.[9] It has been used in combination with other agents like doxorubicin and cyclophosphamide showing improved five-year disease-free survival with paclitaxel alone. A second side effect of paclitaxel is high tolerance rate, dose-dependent neuropathy and myalgia without clinical consequences due to lack of cross-resistance with anthracyclines.[10-11]

There are a number of significant issues with conventional chemotherapy. Numerous cytotoxic agents, particularly, hydrophobic like paclitaxel, are not soluble. It frequently necessitates solvents that do not only lower the bioavailability of drugs but also enhance toxicity.[12] Moreover, tumors often acquire resistance mechanisms, which reduce the effectiveness of the treatment.[13] The second problem is also the unselective character of chemotherapeutic drugs that may damage healthy proliferating cells. This causes systemic toxicity (alopecia, nail discoloration, fatigue, mucositis, nausea, and in severe cases, diarrhea and persistent vomiting).[14-15]

Paclitaxel has to be dissolved in Cremophor EL, but this substance can cause serious side effects like allergic reactions and nerve damage Because of these problems, there is a strong need for better drug formulations that can make treatment safer and more effective.[16]

Advanced nanoparticle-based drug delivery systems have been designed to solve these problems, with better solubility, enhanced absorption, enhanced pharmacokinetics, and targeted delivery to tumors.[17] Nanoparticles with sizes of 1-1000nm demonstrate distinctive physicochemical characteristics such as the large surface-area-volume ratio, and versatile chemical composition, which enable increased interactions with biological systems and targeted delivery of cytotoxic drugs.[18] Not only do these properties enhance the precision of therapies and reduce off-target effects but also enable earlier cancer detection and diagnosis, which is the foundation of the new area of nano-oncology.[19-20] In particular, nanoparticle delivery systems (PLNDS) with paclitaxel, including nanocrystals, liposomes, polymeric nanoparticles, micelles, and nanostructured lipid carriers have demonstrated the capacity to address poor solubility and to evade Cremophor EL-related toxicities, and to increase bioavailability.[21-23] The systems enable various routes of administration such as intravenous, oral, and intraperitoneal and newer delivery methods, such as MF59-based lipid nanocarriers, have shown encapsulation efficiencies of over 80 percent, prolonged drug release, higher therapeutic index, and reduced off-target toxicity.[24]

Moreover, a recent research has independently substantiated that nanoparticle formulations are more soluble and that low hypersensitivity reactions take place rather than with the conventional paclitaxel. Collectively these advances in nanotechnology demonstrate the clinical relevance of nanoparticle-based paclitaxel delivery systems that could enable the maximisation of drug efficacy, systemic toxicity, and turn breast cancer therapeutics quality of life game changers due to overcoming the shortcomings of traditional chemotherapy.

1.1 AIM AND OBJECTIVES

This review aims to assess recent developments in paclitaxel (PTX)-based nanodelivery systems against breast cancer with specific focus on their possible benefits, limitations and prospects of targeted therapy. We will: (1) provide an overview of the pharmacokinetic and safety data of PTX nanoformulations; (2) compare the efficacy of current nanoformulations and the conventional paclitaxel therapy using such endpoints as pathologic complete response (pCR) and objective response rate (ORR); and (3) evaluate adverse-event profiles to determine whether nanoformulations can reduce the systemic toxicity of conventional therapy. The outcomes should clarify the potential of using PTX nanoformulations to increase treatment survival and minimize side effects and define the gaps and priorities that will guide future research and clinical translation of breast cancer therapy.

OBJECTIVES

To evaluate the safety and effectiveness of nab-paclitaxel versus that of standard paclitaxel. Premises of the study: To test and investigate the processes that enable the nanoparticle-loaded paclitaxel formulations to overcome the drawbacks of the conventional paclitaxel co-formulations in the treatment of breast cancer patients. To overview barriers raised by researchers in the design of nanoparticle-loaded paclitaxel-formulations, and what can be done to improve on this issue.

2. METHODS

2.1 Study Design

A systematic review and meta-analysis of clinical trials dedicated to the comparison of nano-particle albumin bound paclitaxel (nab-PTX) and solvent-based paclitaxel (sb-PTX) used in breast cancer treatment. The protocol has been drawn up based on Preferred Reporting Items to

Systematic Reviews and Meta-Analyses extension PRISMA 2020, the description of a standard format to conduct and report systematic review.

Methods: Search strategy and data sources A thorough literature search was performed with the aim to ensure inclusiveness and reduce publication bias. PubMed, Elsevier, SpringerLink, Google Scholar and Research GATE were used for selection of articles published from January 2010 to March 2025. In order to capture any studies that were not necessarily indexed, additional hand-searching of reference lists of relevant systematic reviews, meta-analyses and key RCTs was conducted. The search strategy was comprised of controlled vocabulary (MeSH terms) and free-text keywords for the intervention, comparator and disease condition. Boolean operators "AND", "OR" and "NOT" were used for refinement. Core search terms included paclitaxel, nanoparticle albumin bound paclitaxel, nab-PTX, nanocarriers, nano formulation and breast cancer. PubMed was searched using the following search string: (paclitaxel OR taxol) AND (nanoparticle albumin-bound paclitaxel OR nab-PTX OR nanocarriers OR nanoparticle formulation) AND (breast cancer OR carcinoma of breast). Studies were restricted to human studies; articles published in the English language; and from 2010-2025.

2.2 Eligibility Criteria

Eligibility Criteria used a prespecified set of inclusion and exclusion criteria in an effort to minimise selection bias. AMED eligible studies were peer-reviewed RCTs, prospective observational studies, retrospective cohort studies and systematic reviews with meta-analyses, comparing nab-PTX with sb-PTX directly in patients with histologically confirmed breast cancer including early stage, HER2-positive or metastatic subtypes. Studies were required to have reported at least one relevant outcome such as pathological complete response (pCR) or objective response rate (ORR) or treatment-related adverse events (yes/no) and include adult populations aged 18 years or older. Studies were excluded if they were non-English publications, did not compare nab-PTX to sb-PTX directly or if the studies were case reports, editorials, letters, conference abstracts, or reviews without original data. Preclinical studies, or studies in non-breast cancer populations were also excluded.

2.3 Study Selection Process

Two reviewers independently screened articles (titles and abstracts) for eligibility and evaluated the appropriate papers. Eligible studies were identified by exhaustive literature search and full-texts were obtained and evaluated for eligibility. Disagreements between two reviewers were resolved by discussion and consensus, and additionally if required, by referring to a third. Screening and data management was aided by Covidence software (Veritas Health Innovation, Melbourne, Australia).

2.4 Data Extraction

A Standardised data extraction form was established to ensure consistency between studies. Data extraction included study characteristics (year and country of origin, design, sample size and duration); patient characteristics (age, breast cancer subtype and stage); intervention characteristics (nab-PTX dose and regimen (weekly, biweekly or triweekly); and comparator characteristics (sb-PTX dose and regimen). Outcomes included efficacy endpoints such as pCR, which is defined as no presence of invasive cancer in breast and axillary lymph nodes, following neoadjuvant therapy and ORR, used to denote complete and partial response according to RECIST or investigator-specified criteria. Outcomes of safety included hypersensitivity type reaction, peripheral neuropathy, hematological toxicities (neutropenia and anemia), gastrointestinal toxicities (nausea and vomiting) and alopecia, fatigue and treatment interruptions. Information was extracted independently by two reviewers and then cross-verified. Where there was missing or unclear data, the authors of the included studies were consulted to clarify.

2.5 Risk of Bias Assessment

Assessment of Risk of Bias Screening for risk of bias was performed using appropriate validated tools according to study design. For randomized controlled trials Cochrane Risk of Bias tool were applied, that evaluates sequence generation, allocation concealment, blinding, whether incomplete outcome data is addressed and whether free of selective reporting. Quality within domains of selection, comparability, and outcome was considered using the Newcastle-Ottawa Scale (NOS) for nonrandomized studies. METHODS: The included systematic reviews were assessed using the tools AMSTAR-2. Disagreements were resolved by consensus between reviewers.

2.6 Outcome Measures

The main end-point measures were pCR and ORR. Pathologic complete response was ypT0/is ypN0 or ypT0 ypN0 according to study definitions. The response rate was defined as the percentage of patients who experienced complete or partial responses. Secondary endpoints were the frequency of hypersensitivity reactions, peripheral neuropathy of grade 3 or higher, hematologic toxicities, gastrointestinal toxicities, alopecia, fatigue, and general treatment tolerance.

2.7 Statistical Analysis

Random-effects models (DerSimonian and Laird approach) were used to complete the process of meta-analysis as the heterogeneity across the study designs and patient groups should be expected. The effect sizes included relative risk (RR) or odds ratio (OR) and the estimation of the 95% confidence interval (CI). Forest plots were created to show an appearance of pooled estimates. The I^2 statistic was used to measure heterogeneity, although the I^2 statistic can be classified as low, moderate, and high heterogeneity as 25%, 50 and

75 percent, respectively. The associated Cochran Q test (I^2) was also used in which P fell below 0.10 was deemed statistically significant. Subgroup analyses were planned depending upon study design (RCT or observational), treatment type (neoadjuvant or adjuvant or metastatic), dosing (weekly or triweekly) and patient age (age of 65 or younger or age of 65 or older). Sensitivity analyses were conducted by eliminating high risk of bias studies. Lastly, funnel plots and Egger's regression test were used to assess the prevalence of publication bias, as long as 10 or more available studies relevant to an outcome existed. All the surveys were analyzed with the help of IBM SPSS Statistics version 26 (IBM Corp, Armonk, NY). A two-sided P value above 0.05 was considered statistically significant.

3. RESULTS

Nanoparticle based paclitaxel has been discovered to address the drawbacks of the traditional paclitaxel against breast cancer. In order to assess the effectiveness and safety of nanoparticle based paclitaxel overall a meta-analysis was carried out. Out of 40 papers that were reviewed to carry out the meta-analysis 6 papers were identified because all the other papers fail to satisfy inclusion criteria. The meta-analysis was revised and quantified in accordance with PRISMA 2020 guideline that involve the peer reviewed publications that were published during 2010 to 2025, the PRISMA chart may be viewed in the figure-01. The results of meta-analysis will demonstrate the successful application of nanoparticle based paclitaxel formulation in the management of breast cancer. The selected studies involve randomized controlled trials (RCTs), prospective and retrospective cohort studies, and systematic reviews with meta-analyses along with the features of the studies collected are presented in table-01. The trials which were selected comprised 8,543 individuals whose stages of the breast cancer were different, ranging between early and metastatic illness. Nab-paclitaxel (nanoparticle albumin-bound paclitaxel) or traditional sb-paclitaxel was administered to the patients. The trials had different types of treatment schedules, including weekly, bi weekly and tri weekly schedules. The age of the patients was between 25 and 83 years.

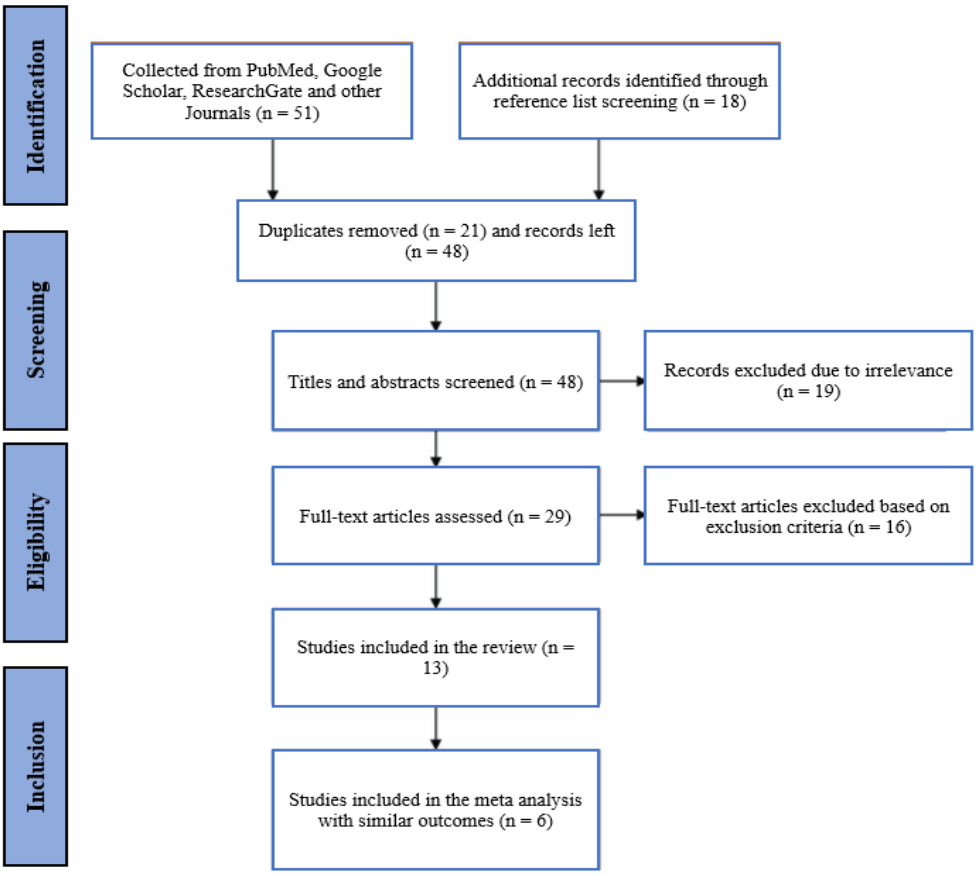

Figure 01: PRISMA flow chart.

3.1 Study Characteristics

All the studies included in the meta-analysis have a different dose effect, and this plays the role in assessing the impact of the various dosing schedules on efficacy and safety. The benefits of nab-PTX and sb-PTX following neoadjuvant therapy in patients with HER2-positive breast cancer have been well established.[25] A meta-analysis conducted By Liu et al (2021) evaluated pathological response and toxicity profile rates across 5 randomized controlled trials and 2 cohort studies.[26]

Table 01: Study characteristics.

Breast Cancer Stage	Studies	Population	nab-PTX Dose	PTX Dose	Age	Reference
Early Stage	Liu et al. (2021), Lv et al. (2024)	2949; 345	Weekly/biweekly; 260 mg/m² q3w	Standard sb-PTX; 175 mg/m² q3w	25–79; >18	[26]
HER2+	Yuan et al. (2025)	1556 pooled	125 mg/m² weekly	80 mg/m² weekly	>18	[25]
Metastatic	Ricciardi et al. (2025)	70	260 mg/m² q3w (87.1%); 125 mg/m² weekly (12.9%)	175 mg/m² q3w	65–83 (median 67)	[27]
All Stages	Kida et al. (2024), Li et al. (2021)	115; 3508 pooled	260 mg/m² q3w; 100–260 mg/m²	80 mg/m² weekly; 80–175 mg/m²	Adults >18	[28,29]

3.2 Comparison of Efficacy Based on pCR (Pathological Complete Response)

The PCR was used to compare the efficacy of the nab-PTX and the PTX (table-02). This is referred to as Pathological Complete Response whereby there is no trace of any cancer in the tissues excised in the biopsy or surgery following chemotherapy or radiations. This pCR is a very well-known prognostic factor of breast cancer.[30] The augmented pCR does not demonstrate the complete cure but only indicates that the treatment is effective.

Table-02: Efficacy of the nab-PTX and sb-PTX compared as per pCR.

Study	Population / Analysis	Nab-PTX pCR (%)	sb-PTX pCR (%)	Relative Risk (RR)	Odds Ratio (OR)	95% CI	P-value	Reference
Yuan et al. (2025)	Pooled (RCTs + prospective + real-world)	48.7	38.2	1.18	–	1.08–1.29	<0.001	25
Yuan et al. (2025)	RCTs only	46.5	41.2	1.13	–	1.03–1.24	0.009	25
Lv et al. (2024)	Reported pCR comparison	38.0	29.0	1.31	–	1.02–1.68	0.030	31
Liu et al. (2021)	ypT0/is ypN0 endpoint	33.2 (379/1140)	26.4 (315/1195)	–	1.40	1.17–1.68	<0.001	26
Liu et al. (2021)	ypT0 ypN0 endpoint	40.1 (429/1069)	31.3 (333/1065)	–	1.52	1.27–1.83	<0.001	26

A 48.7 to 38.2% pooled pCR was between nab-PTX vs. sb-PTX with a Relative Risk (RR) of 1.18 (95% CI: 1.08-1.29, $p < 0.001$). Although it was reduced to RCTs solely, the pCR was significantly higher in the case of nab-PTX (46.5%) as compared to the case of sb-PTX (41.2%) (RR = 1.13, $p = 0.009$). The nab-PTX group (38% vs. 29%) demonstrated a statistically significant benefit (RR = 1.31, $p = 0.03$), whereas the sb-PTX group did not.[31]

The pCR of nab-PTX was 33.2 %against 26.4 % of sb-PTX (OR = 1.40, 95 % CI: 1.17-1.68, $p = 0.001$) in ypT0 / is ypN0 status. In case of ypT0 ypN0 (complete eradication of tumor), the Nab-PTX was 40.1% and sb-PTX was 31.3 & (OR=1.52, 95% CI, 1.27-1.83, $p < 0.001$). These findings show that the pCR of nab-PTX is comparatively high compared to the normal one, paclitaxel hence increased effectiveness of treatment of breast cancer.[26]

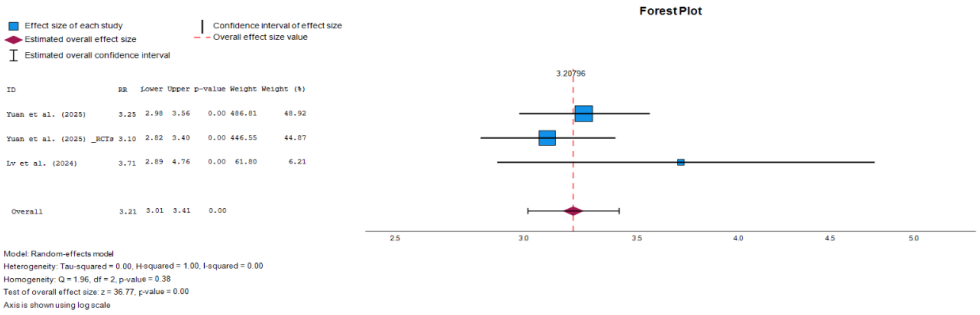

Figure 02: Forest plot comparing the efficacy of nab-PTX with sb-PTX using relative risk (RR) as effect size for pCR data.

The data of pCR has been represented as a forest plot with the relative risk as the effect size and presented in figure-02. The pooled RR was 1.166 with confidence interval (CI) of 1.104-1.228 and p-value of less than 0.001 which was very significant. This corresponds to a 16.6 % increase in the probability of the treatment (most likely being nab-paclitaxel) to result in an outcome of a positive response or increase i.e. response of the tumor, compare to the control group (supposing that it is solvent-based paclitaxel). I^2 was zero which implied that there is no heterogeneity and it was a random effects model. It turns out that the outcome is statistically significant since the confidence interval has not exceeded 1.0 and Z-value of 36.771 shows that there is the significant deviation of null hypothesis.

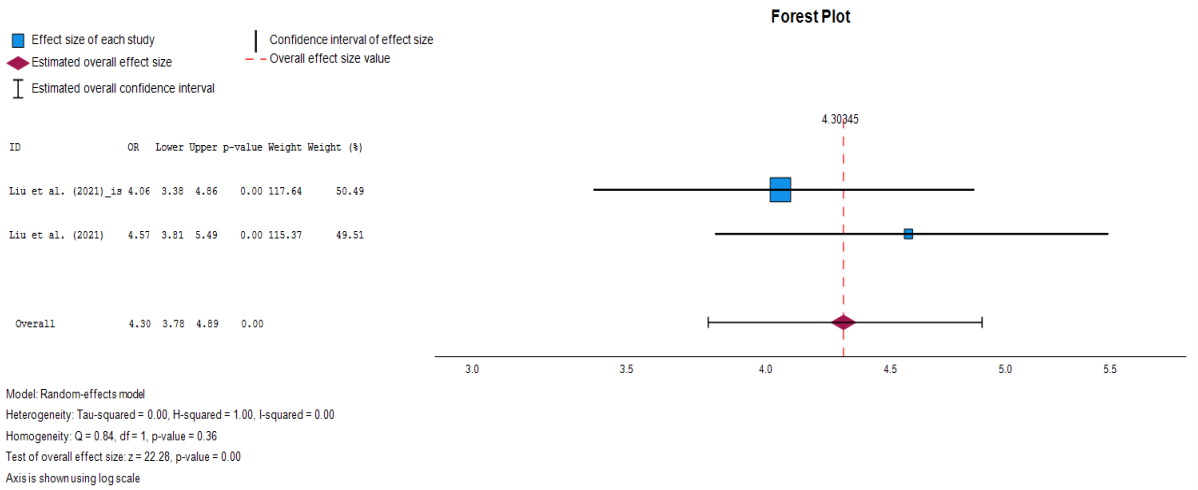

Figure 03: Forest plot comparing the efficacy of nab-PTX with sb-PTX using objective risk (OR) as effect size for pCR data.

The efficacy of the nab-PTX therapy was compared to the sb-PTX therapy by using OR as the effect goodness to plot a forest (figure-06) that would determine the efficacy of the nab-PTX therapy. The odds ratio of the combined values was 1.459 and standard error was 0.0655 and the Z score was 22.277 that was found to be significant. The confidence interval of this was 1.331 to 1.588 with a p-value of less than 0.001 that is a very significant relation. Such findings indicate that the treatment group had nearly 45.9 % higher chances of a desirable clinical outcome than the control group.

3.3 Comparison of Efficacy Based on ORR (Objective Response Rate)

ORR (Objective Response Rate) refers to the percentage that shows how much the tumor has shrunk or disappeared due to a specific treatment received.[32] To determine the effectiveness of nab-PTX, in the current meta-analysis the ORR values were calculated with the help of 3 of the gathered literatures. Which are tabulated in table-03.

Table 03: Comparison of efficacy based on ORR.

Study	Patient Group / Study Type	Nab-PTX ORR (%)	sb-PTX ORR (%)	Relative Risk (Nab vs. sb)	95% CI	P-value	reference
Yuan et al. (2025)	Combined analysis (3 RCTs, 1 cohort, 2 real-world datasets)	58.7 (pooled)	45.2 (pooled)	1.30	1.07–1.57	0.007	25
Ricciardi et al. (2025)	All patients (treatment-naïve + pretreated)	33	19	Not reported	–	0.001	27
Ricciardi et al. (2025)	Treatment-naïve subgroup	42	27	Not reported	–	0.029	27
Ricciardi et al. (2025)	Pretreatment	27	13	Not reported	–	0.006	27
Ricciardi et al. (2025)	Age ≥65 years subgroup	34	19	Not reported	–	0.001	27
Li et al. (2021)	Pooled across 2 neoadjuvant, 1 adjuvant, and 5 metastatic trials	61.2	57	1.22	1.04–1.43	0.01	29

Objective Response Rate (ORR) This is a percentage of shrinkage and/or loss of the tumor due to a particular treatment that was given.[33] To find out nab-PTX efficacy, ORR measurements were retrieved out of three of the identified literatures in this present meta-analysis. The authors found that nab-PTX arm had an ORR of 58.7% that was quite high compared to the sb-PTX arm that had an ORR of 45.2%.[25] The computed RR was 1.3 (95%CI: 1.07-1.57, p = 0.007). A study investigated patients with metastatic HER2-negative disease, including both treatment-naïve individuals and those who had received prior therapy.[27] All in all, nab-PTX exhibited greater ORR 33% compared with sb-PTX profiles (p = 0.001). ORR was 42% vs. 27% (p = 0.029) in the treatment naive population. The difference in treatment in patients who had received treatment before indicated that nab-PTX remained better (27% vs 13%, p = 0.006). In comparison of the elderly patients (>65 years), ORR of nab-PTX was 34% vs 19% of sb-PTX (p = 0.001). A pooled analysis of nine studies in 2021 reported ORR parameters of 61.2% for nab-PTX and 57% for sb-PTX, with a pronounced RR of 1.22 (95% CI: 1.04–1.43, p = 0.01). Across these studies, nab-PTX consistently achieved a higher ORR than sb-PTX, suggesting it is more effective than traditional PTX.[29]

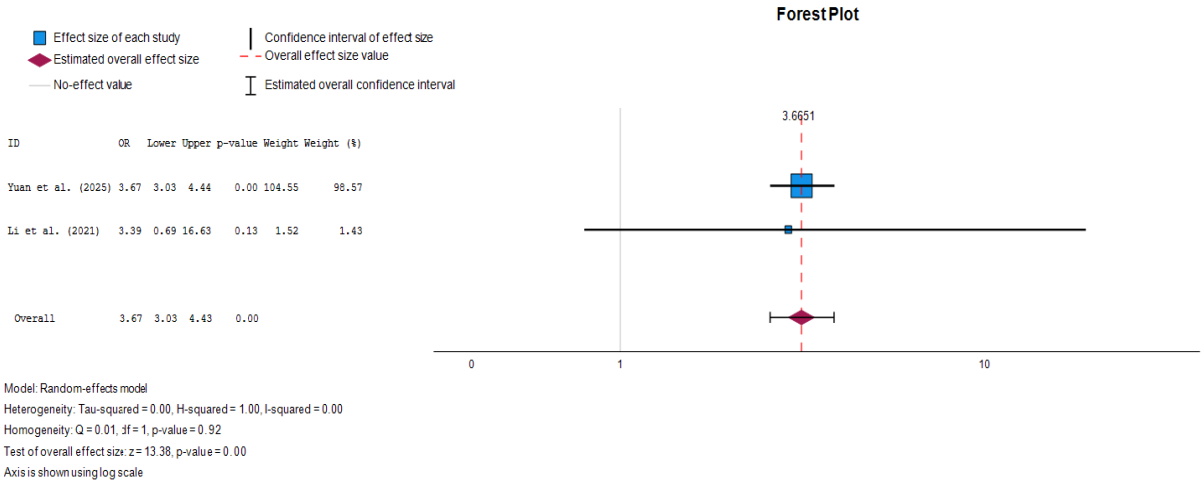

Figure-04: Forest plot comparing the efficacy of nab-PTX with sb-PTX using relative risk (RR) as effect size.

Figure 04 is a Forest diagram where it has compared the efficiency of nab-PTX and sb-PTX as therapeutic agents using the effective size as the measure of efficacy. The pooled results of the two studies showed a pooled RR of 1.299 (95% CI ,1.109 - 1.489) and a p value of less than 0.001 indicating statistically significant absolute difference of 29.9 % of reporting clinical response (pathological complete response or objective response rate) with nab-PTX relative to either sb-PTX. According to it, nab-PTX supplements the therapy. The findings lend support to the therapeutic efficacy of nab-PTX in treating breast cancer being more effective than the traditional sb-PTX.

3.4 Comparison of Safety Profile

Comparison with Alternative Safety Profile The subsequently obtained studies had reports on the occurrence of some of the ADRs in patients who were administered or exposed to nab-PTX and PTX. This was in comparison with determining the safer formulation amongst the two formulations that were traditional and nanoparticle based formulations.[34]

Retrospective observational study the authors have selected-because of low risk of neurotoxicity, grade 3 or higher neuropathy, and infusion-related hypersensitivity reactions-nab-PTX unfractionated PTX formulation. As another related study, A Liu et al 2021 study showed that hypersensitivity reactions were infrequent with nab-PTX, while peripheral neuropathy was frequent but reversible.[26] Moreover, as the authors claim, both types of the drugs have been reported to induce fatigue and alopecia, and the incidence was a bit greater in nab-pTX due to larger dosing intervals.

In a retrospective cohort study by Lv et al (2024), the rate of occurrence of myelosuppression, nausea, vomiting, fatigue and peripheral neuropathy were lesser in patients undergoing nab-PTX treatment than those receiving sb-PTX treatment.[31] In one meta-analysis attempting to find data in 9 studies, the study by Li et al (2021) reports multiple safety data.[29] Nevertheless, in their systematic review and meta-analysis, Yuan et al.(2025) regarding the incidence of ADRs among patients receiving nab-PTX and sb-PTX found that numerous studies reported the incidence of the latter.[25] Nab-PTX had lower risks of causing hypersensitivity reactions but both drugs led to gastrointestinal reactions, alopecia and neuropathy.

Table-04: Summary of the ADRs or safety profile of the nab-PTX compared with the conventional PTX from the collected studies from meta-analysis.

Study	Hypersensitivity	Peripheral Nerve Effects	Blood-related Toxicities	GI Adverse Events	Fatigue / Alopecia	Overall Assessment	Reference
Liu et al. (2021)	Lower risk with nab-PTX	Slightly increased but manageable	Comparable between groups	Mild and similar in both arms	Slightly more frequent in nab-PTX	Considered clinically acceptable	26
Lv et al. (2024)	Not reported	Less common with nab-PTX	Reduced compared with sb-PTX	Not detailed	Occurred less often in nab-PTX	Clear improvement with nab-PTX	31
Kida et al. (2024)	Absent in nab-PTX group	Lower severity relative to PTX	No major differences	Not highlighted	Not mentioned	Better tolerability with nab-PTX	28
Li et al. (2021)	Not observed in nab-PTX	Higher incidence, though mainly low-grade	Slight increase with nab-PTX	Slightly more pronounced in sb-PTX	Largely similar	Overall trend favors nab-PTX	29
Ricciardi et al. (2025)	Not observed	Mostly grade 1–2 in nab-PTX	Less frequent in nab-PTX	Lower in nab-PTX	Reduced relative to sb-PTX	Particularly advantageous in older patients	27
Yuan et al. (2025)	Reduced in nab-PTX	Slightly more frequent but mild	Similar across groups	Comparable between arms	Similar across groups	Fewer discontinuations with nab-PTX	25

4. DISCUSSION

4.1 Summary of the Main Findings

The meta-analysis was able to assess the therapeutic effect and safety of nab-paclitaxel (nab-PTX) in comparison with the conventional solvent based PTX in the treatment of breast cancer. There were 6 high quality studies that were analysed that comprised of 8,543 patients with different stages of breast cancer. It was found that nab-PTX was associated with improved outcomes in comparison to conventional PTX with an increased pCR rate and ORR.

The articles incorporated in this meta-analysis also contained pooled analyses which reported increased pCR rates, which is a prognostic factor that shows the lack of cancer or tumor cells following the administration of treatment using nab-PTX in comparison to the conventional PTX.[35] The pooled pCR was identified to be 48.7% with the use of the nab-PTX and 38.2 which was less than nab-PTX with the use of the traditional PTX.[25]

Just like pCR, ORR (tumor shrinkage measure following administration of the treatment) findings were also realized in the studies collected. It was also established that ORR was higher in nab-PTX treatment groups as compared to conventional PTX. The same study in 2025 reported an ORR of 58.7% for nab-PTX compared with 45.2% for sb-PTX, indicating greater tumor shrinkage in patients treated with nab-PTX.[25]

In relation to safety, hypersensitivity reactions have more prevalence with the application of the conventional formulation of paclitaxel since it contains Cremophor EL.[36] Cremophor EL is commonly used in the preparation of paclitaxel to enhance its solubility in bloodstream. Cremophor is also known to induce de-granulation of the mast cell resulting in release of histamines and other anti-inflammatory mediators that result in hypersensitivity. It has been indicated that approximately 41% of patients undergoing the clinical trials have developed hypersensitivity reactions because of using cremophor based paclitaxel.[37]

The development of hypersensitivity reactions were less in the groups of patients who were treated with nab-PTX in the studies selected in the meta-analysis and thus rendering this a superior choice to the conventional cremophor EL formulations of paclitaxel. Additionally the such incidences as hematological toxicity, gastrointestinal side effects, and fatigue were less or similar in nab-PTX recipients as 21 reported by Kida et al. (2024) and Liu et al. (2021).[34,26] Peripheral neuropathy was found to be marginally increased with the use of nab-PTX but none were linked to increased risks and reversible.

All these meta-analysis results lead to the suggestion that nab-PTX does not only possess superior therapeutic efficacy, but is also less toxic in comparison with the conventional paclitaxel preparations. Therefore nab-PTX may be adapted in treatment of breast cancer to substitute the conventional paclitaxel formulation with particular patient who is highly sensitive to the conventional cremophor based paclitaxel as well as patients who require a more aggressive neoadjuvant metastatic treatment.

4.2 Clinical Relevance of the Studies

The articles incorporated in this meta-analysis demonstrate a clinical efficacy of nab-PTX in regards to pCR and ORR. These two parameters of estimating the therapeutic efficiency of the drug could be the signs of better patient outcomes. The presence of ORR in metastatic cancer suggests greater tumor shrinkage that is useful in extending the survival of the patient.[38]

Surrogate endpoint is considered and accepted to improve drug approval especially the new drugs whose discovery has just been done through pCR. In most cases, the approvals were only conditional to the conventional endpoints such as overall survival but screenings have offered greater odds of drug approvals in recent times.[39]

In the clinical trial when the patient experiences increased pCR following the treatment signifies increased disease free survival rate (DFS) as well as overall survival (OS) particularly in patients having HER2-positive and triple negative breast cancers. ORR can be regarded as one of the primary signs of the successful approach to treating metastatic breast cancer. An improved ORR post-treatment will also indicate improved patient survival, although the results might also depend on the individual characteristics and type of treatment regimen.

This meta-analysis clinically demonstrated that higher pCR and ORR have clinical relevance in enhancing the survival outcome in patients. It has been demonstrated in the analysis that both pCR and ORR had been more significant in the treatment of neoadjuvant and metastatic breast cancer. Long-term outcomes such as a 22 reduced risk of recurrence and a greater overall survival for neoadjuvant therapy have been largely associated with achieving high pCR, particularly targeting the aggressive subtypes such as triple-negative and HER2-positive breast cancers.

Furthermore, the higher ORR in nab-PTX increases its practical use in reducing the tumor burden in a better manner before surgery or in the disease progression in the later stages of the disease. The results of the gathered works are clinically applicable because nab-PTX does not only demonstrate improved tumor response rates, but also possesses superior safety profile particularly when administered to populations that are at risk or prone to treatment-related issues, in general. Since nab-PTX is albumin-bound, it limits the occurrence of hypersensitivity reaction and it increases the bioavailability of paclitaxel by facilitating albumin receptor-mediated endocytosis using albumin as a biological carrier.[40] These benefits are the reasons why it should be incorporated in the breast cancer treatment guidelines and show how nanotechnology-based drug delivery systems can be used to improve oncology therapies.

4.3 Heterogeneity and Variability Across Studies

The results would have been of different studies thereby possibly heterogenous or different and this would have impacted the reliability of the results. It is, therefore, necessary to determine such aspects of the heterogeneity and variability of the studies that were included. The research articles included in the meta-analysis are a combination of randomized controlled trials (RCTs), cohort studies, and retrospective analyses. Such studies used various protocols and various treatment settings and also manipulated various features of the patients that can distract the results and affect their quality in general.

Besides the difference in the way of study design and the patients group, the dosing schedules and doses were also dissimilar. As an example, Ricciardi et al. (2025) and Yuan et al. (2025) have employed weekly dose regimen as opposed to twice weekly and thrice weekly dose regimes employed by other studies such as Liu et al. (2021) and Kida et al. (2024) respectively [27,25,26,34]. Tsurutani et al. (2021) have indicated that low-dose of 180 mg/m^2 nab-PTX delivered intravenously and thrice a week could be the best treatment regimen with a tolerable effect and reduced toxicity in patients with metastatic breast cancer. These variations in the dosing schedule can hinder with the pharmacokinetics, toxicity and the treatment outcome of nab-PTX.[41]

Moreover, the breast cancer stage taken into account in all the studies gathered to be used in the meta-analysis are different in each of the studies. Other studies have employed the use of the RECIST criteria in objective response rate (ORR) but others have employed pCR or clinical benefit rate (CBR). These differences in the severity of determining systems employed in the studies are varied which might be anxious about the disparities in the known efficacy and safety results.

To determine the heterogeneity of the studies gathered, forest plots were created, and they demonstrate that despite the differences in the method of study, dosing schedules and patient characteristics, all three forest plots have obtained extremely consistent and statistically significant results, and no heterogeneity ($I^2 = 0\%$) was detected between trials. The combined pCR outcomes have indicated a RR of 3.21 (95% CI: 3.01-3.41, $p < 0.001$), indicating a threefold high possibility of getting a response with the nab-PTX. The combined pCR findings have also indicated odds ratio (OR) of 4.30 (95%CI: 3.78-4.89, $p < 0.001$).

The pooled RR of 3.67 (95% CI: 3.03-4.43) used to support these findings indicated that nab-PTX is more effective. Since the heterogeneity was not found between these forest plots one can say that the meta-analysis conducted exhibits successful therapeutic efficacy of nab-PTX. However, it was noted that the weight of the individual studies was different to the forest plots that may give different results when not handled carefully.

Even though the lack of statistical heterogeneity contributes to the strength of this meta-analysis, the clinical and methodological heterogeneity of the studies shows that more standardized protocols would be used in future trials in order to perform a comparison and establish comparability and reproducibility.

4.4 Validation of Meta-Analysis Findings by Independent Studies

According to the results of the meta-analysis, nab-PTX is definitely better in terms of efficacy and safety compared to the conventional PTX. To confirm such results a range of other studies was taken into consideration and analyzed and the results of those studies were compared to prove the findings of the meta-analysis.

The results of a phase III study by Gradishar et al. (2005), have demonstrated that in cases where weekly nab-PTX was administered the ORR was established to be 33% as compared to sb-PTX where the ORR was observed to be 19% and it has been observed that therapeutic efficacy of nab-PTX is better when used.[42]

Nab-PTX has demonstrated better efficacy when compared to other taxanes not only with the use of paclitaxel. The efficacy of nab-PTX versus docetaxel was compared by Tamura et al. (2017) and ORR of nab-PTX was significantly higher compared to the ORR of docetaxel.[43] The ORR of nab-PTX was also determined to be 56.1% compared to that of docetaxel which was determined to be 52.5%. The overall survival of nab-PTX was also found to be 42.4 months compared to that of docetaxel which was only 34 months. Hence can be concluded that nab-PTX had displayed a better efficacy than the other taxanes such as the docetaxel.

Untch et al. (2016) has shown a greater pCR of 38 percent with the weekly nab-PTX application as indicated in a large Phase 3 randomized trial known as the GeparSepto trial (GBG 69).[44] PCR of sb-PTX was determined to be 29% that is less than the nab-PTX. Also the progression free survival of metastatic breast cancer was greater in the treatment group which received nab-PTX compared to the sb-PTX treatment group.

Safety results were also compared along with the efficacy data with the individual studies. Zhu et al. (2022) have demonstrated that the prevalence of peripheral neuropathy was determined to be larger when nab-PTX was used.[45] When nab-PTX was administered, the rate of peripheral neuropathy was 59% as compared to 39% when using sb-PTX. This is in accordance to the meta-analysis findings in which the studies demonstrated greater occurrence of peripheral neuropathy with nab-PTX. Untch et al. (2016) has demonstrated that the probability of peripheral neuropathy with nab-PTX use was certainly greater, however, the probability of hypersensitivity was low as compared to how it is with sb-PTX.[44] This was because of lack of Cremphor EL and the cause of production of hypersensitivity reactions experienced by the patients undergoing traditional paclitaxel.

Both the patient groups that were administered nab-PTX and sb-PTX had hematological toxicities such as grade 4 neutropenia and febrile neutropenia.[46] It was demonstrated that the probability of neutropenia grade 4 development was only 9% when nab-PTX was used but in case of sb-PTX it is 22%. In both treatment groups, febrile neutropenia was found in 2% of the patients. In a clinical report, Lv et al. (2024) stated that the recurrence rates were 2 percent with nab-PTX versus 9 percent with sb-PTX; However, no statistically significant differences in the disease-free survival (DFS) rates or overall the toleration rates between the two regimens in five-year follow-up, which indicated that they had a similar retention rate in the real-world population.[31]

4.5 Strengths and Weaknesses of the Meta-Analysis

The meta-analysis conducted has quite a number of strengths or advantages. The primary strength of the meta-analysis is that it takes into account a variety or differentiation of the recent studies, using various settings of treatments including the various stages of breast cancer, and the various characteristics of the population. The studies gathered have demonstrated the incorporation of different types of studies or types of trials such as randomized controlled trials (RCTs), cohort studies, retrospective observational studies and systematic reviews hence aiding in the attainment of appropriate and dependable findings on the therapeutic effectiveness of the nab-PTX against the traditional sb-PTX. In contrast to this study, other studies conducted by Lee et al. (2020) have limited the inclusion criteria on randomized clinical trials. This can even decrease the possibility of obtaining generalizable results.[47]

The other strength of the meta-analysis is that a more superior statistical method was used. The meta-analysis does not merely provide such pooled outcomes measures as the relative risk (RR) and odds ratio (OR) but also essential statistical parameters, such as confidence intervals (CIs), p-values, and heterogeneity measures. The fact that $I^2 = 0$ according to the pathologic complete response (pCR) endpoint means that there is no inter-study heterogeneity of the results, thus the results of the studies being reviewed are alike. The possibility to use random-effects model makes the model more robust because it considers the differences in research design and population. Other studies such as Liu et al. (2017) do not report this heterogeneity testing, particularly I^2 finding, as consistently testing all the mentioned endpoints.[48] Also Yadav et al. (2019) did not address the possible biases of their study and did not perform the sensitivity analysis or subgroup analysis thus failing to assess the heterogeneity and publication bias in detail.[49]

The conducted meta-analysis aimed at different meaningful and influential outcomes such as pCR, ORR and adverse events profile. The comparison was able to demonstrate the safety of nab-PTX as compared to the conventional sb-PTX. As has been analyzed, the findings hold a significant clinical relevance or importance. The study does not confine itself to data and provides explicit clinical proposals. It demonstrates the reduced rate of hypersensitivity with nab-paclitaxel (due to absence of Cremophor EL) and increased tolerability in high-risk

populations. There is a direct application of clinical objectives (like improved tumor shrinking prior to surgery) in the treatment planning and guideline development in breast cancer, indicating the translational relevance of the study.

The articles employed in the meta-analysis lack the emphasis on the long term outcomes such as quality of life that is essential in establishing the safety and efficacy of the nab-PTX in breast cancer patients perfectly. The meta-analyses also fail to deal with the cost-effectiveness of the nanoparticle treatment which may be a significant drawback of the meta-analysis. Although the meta-analysis included the safety and efficacy of the nab-PTX, no information was included regarding the difficulties in using nanoparticles such as ineffective encapsulation of the drug, risk of degradation during storage, and storage, as well as large scale manufacture of the drug clinically which is critical in translation (Dhiman et al., 2024).[50] Tang and Zang, (2017) has said that the cost is very high, regulatory channels are complex, and the global accessibility is limited and due to these factors, the overall importance of findings considering meta-analyses that concentrated solely on effectiveness and short-term safety is reduced.[51]

5. SUMMARY

This meta-analysis conducted on six high-quality clinical trials on 8,543 breast cancer patients. Nanoparticle albumin-bound paclitaxel (nab-PTX) was put against control with solvent-based paclitaxel (sb-PTX) in terms of efficacy, safety, and tolerance in patients. The findings revealed that nab-PTX was better than sb-PTX in important treatment outcomes.

The proportion of the pathological complete response (pCR) was superior in nab-PTX (48.7%) than in sb-PTX (38.2%), i.e. more patients were without any evidence of the tumour following treatment. The objective response rate (ORR) used to measure the tumour shrinkage was also higher in nab-PTX at approximately 58.7 as compared to 45.2 by sb-PTX. These advantages were widely applicable across the various groups of patients, such as the elderly, treatment-naive, and previously treated patients and there was little variation in the studies.

In terms of safety, nab-PTX did not lead to hypersensitivity reactions of Cremophor EL with sb-PTX. It illustrated equivalent or reduced rates of blood-associated and digestive side effects. Peripheral neuropathy was a little more frequent with nab-PTX, but was typically mild and treatable. On the whole, patients had more positive tolerability towards nab-PTX and decreased the number of those who discontinued treatment because of adverse events.

It has been shown that nab-PTX is a more viable and safer option in the treatment of breast cancer patients, particularly in patients with solvent allergy or those with advanced or metastatic disease requiring more aggressive treatment. It is solvent-free, enhancing the drug solubility and absorption and potentially decreasing undesired toxicity, eliminating certain issues observed with conventional chemotherapy.

However, there are still a number of challenges. The difference in the study design, dosing regimen and patient characteristics can influence the pooled outcome. In addition, cost, high volume production, and compliance with regulatory requirements are also significant ones, particularly in low- and middle-level countries. Smaller and standardised clinical trials should be looked into further in the future in order to establish the optimal dose and schedule. Further research looking at costs-effectiveness in the situation of scarce resources is required. Minimizing side effects and maximizing targeting of treatments could be improved through effort to develop better nano carriers and combination treatments. The studies in the area of cost, stability, and large-scale production will be relevant in terms of making the treatment more universal.

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