Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/6t7pre51

EVALUATING THE EFFICACY OF NAB-PACLITAXEL AS NEOADJUVANT THERAPY FOR HER2+ BREAST CANCER

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Abstract:
This systematic review and meta-analysis evaluate the efficacy and safety of nanoparticle albumin-bound paclitaxel (nab-paclitaxel) as a neoadjuvant therapy for HER2+ breast cancer. The analysis compared nab-paclitaxel with conventional paclitaxel treatment, specifically in the context of pathologic response rates and clinical outcomes in different subtypes of HER2+ breast cancer, with a focus on aggressive subtypes like triple-negative breast cancer (TNBC). Our findings suggest that nab-paclitaxel significantly enhances pathologic response rates (ypT0/N0) and improves clinical outcomes compared to paclitaxel, particularly in TNBC cases. Despite its promising results, nab-paclitaxel's safety profile, including increased sensory neuropathy at higher doses, warrants careful consideration. The study also highlights the need for further randomized controlled trials to confirm its superiority over conventional therapies and to explore its potential synergistic effects with other treatments. The role of biomarkers, such as SPARC, in enhancing nab-paclitaxel's specificity for targeting HER2+ breast cancer cells requires further investigation. This meta-analysis supports nab-paclitaxel as a potential alternative to standard neoadjuvant treatments for high-risk or metastatic HER2+ breast cancer, offering new avenues for improved therapeutic strategies.

Keywords: HER2+ breast cancer, Nab-paclitaxel, Neoadjuvant therapy, Triple-negative breast cancer (TNBC), Pathologic response

INTRODUCTION

The cancer with HER2+ is the most prevalent female cancer in all the world and it is among top causes of cancer deaths [1]. In the general clinical practice, neoadjuvant systemic therapy has emerged as a popular treatment of cases with active and advanced HER2+ locally [2]. Patients that were treated by the use of the Neoadjuvant system and that showed a total pathologic response after receiving a treatment had a much better survival than those cases, which did not receive a complete pathologic response after treatment [3,4]. Taxes play a role in the treatment of lymph +ve adjuvant or high-risk, HER2 +, gland -ve [5] and better clinical response [6]. Paclitaxel is one of the most popular drugs which are used in HER2+ treatment. Neoadjuvant Paclitaxel led to increased tumour response and improved survival results in those cases presenting pathologic response [7 -13]. Paclitaxel, in its turn, has a soluble- toxin known as Poly ethylated castor oil and ethanol, thus creating hypersensitivity reactions and strong peripheral neuropathy. [14, 15]
The clinic should administer paclitaxel to the cases with long-term steroid and antihistaminic prophylaxis.

The nabpaclitaxel is a novel nanometer-scale particle albumin-bound paclitaxel developed first as an anti-polyethylated castor oil poisoning agent [16]. It was believed that albumin delivery leads to an increased delivery of nab-paclitaxel to the tumor [17] and altered profile of nab-paclitaxel tolerance compared to paclitaxel when given at the equivalent dose and a shorter delivery schedule, with no accompanying administration of medications [16]. The response rate was found to be higher and the disease progression was delayed in patients who were treated with nab-paclitaxel at a dosage of 260 mg/m 2 than the patients treated with paclitaxel at dose of 175 mg/m 2 in a large phase III trial which compared the nab-paclitaxel with paclitaxel in metastatic disease occurrences of breast cancer. Although the safety aspects of nab-paclitaxel remained acceptable in most of the preceding trials [19-21], there is still no direct head-to-head comparison of nab-paclitaxel and paclitaxel that can be done to make any judgment. Furthermore, nab-paclitaxel is not yet known to be equal or even better to standard HER2+ therapy. Safety and efficacy of nab-paclitaxel-based regimens have been investigated in advanced or active HER2+ cases in two phase II trials and two randomized trials. Nonetheless, the synthesis of clear inferences on the value of nab-paclitaxel in neoadjuvant therapy has been challenging because of a number of factors including: 1) most of such studies are single-arm, randomized phase II studies that often have small sample sizes; 2) some of them cover subcontinental populations; 3) the studies differ in terms of schedules, dosing and combinations of nab-paclitaxel regimes; 4) and they adopt varying definitions of pathologic response. Consequently, we performed a meta-analysis of all the neoadjuvant studies that were done using paclitaxel and nab-paclitaxel to: 1) evaluate the effectiveness of nab-paclitaxel in both general and specific HER2+ sensitive cases and 2) compare the toxicity and effectiveness of nab-paclitaxel to the other standard taxanes.

AIMS AND OBJECTIVES

Efficacy of nanoparticle albumin-bound paclitaxel as neoadjuvant therapy of HER2+ breast cancer by a meta-analysis.

MATERIALS AND METHODS

Choosing of research:

The following Medical Subject Headings (MeSH) parenchyma of the breast neoplasms were compared and the same following key words (1) HER2; (2) nab-paclitaxel OR nanoparticle paclitaxel; (3) neoadjuvant OR (as per the Preferred Reporting Meta-Analysis Index,then the subject was extended using the subject related topics, in order to obtain the relevant summaries. Such a search strategy was used on year-to-year basis, with no limitation in language, and all retrieved comparative studies have been in the English language.

Data extraction

Two researchers follow-through search, appraisal and publish the following information pertaining to each study as it was pre-determined: first author, date of issue, demographics, study composition, number of studies, type of therapy and final point information. Disagreement was covered by the reviewing and settling of documents to be debated on.

Inclusion and removal criteria:

Studies included in the analysis have to fulfill all the following criteria:

1. Non-metastatic HER2+ cases in which pathologic response was documented after performing a neoadjuvant regimen, which contained nabpaclitaxel.
2. The possibility to read the whole article or conference abstract.
3. Distinct pathologic response definition (ypT0/is ypN0, ypT0 ypN0, or ypT0 ypN0/+).
4. The number of qualifying cases responding to the survey exceeded 30 cases.
5. At least 9 doses of nab-paclitaxel per week, or nab-paclitaxel doses of three cycles every three weeks

A study would not be possible due to any of the following:

1. Research on adjuvant chemotherapy or metastatic HER2+;
2. the endpoint of a therapy response: pathologic is not used;
3. It is studies that do not contain critical information.

Table 1: Paclitaxel With Different Parameters

TOXICITY	NO OF EVENTS		OR	95%CI	P VALUE
	NAB - PACLITAXEL	PACLITAXEL			
NEUTROPENIA					
ANY VALUE	672	609	1.449	1.162	0.001
VALUE >3	471	437	1.294	0.70	0.407
LEUCOPENIA					
ANY VALUE	642	619	1.213	0.891	0.178
VALUE >3	308	295	1.066	0.86	0.55
INCREASED ALANINE AMINOTRANSFERASE					
ANY VALUE	364	379	0.907	0.73	0.35
VALUE 3	16	17	0.655	0.11	0.63
INCREASED ASPARTATE AMINOTRANSFERASE					
ANY VALUE	250	235	10.89	0.87	0.45
VALUE >3	6	6	0.99	0.334	0.991
SENSORY NEUROPATHY					
ANY VALUE	725	575	2.09	1.01	0.045
VALUE >3	78	22	3.76	2.34	<0.001
NAUSEA					
ANY VALUE	615	612	0.995	0.82	0.93
Value >3	28	27	1.031	0.6	0.91

Toxicosis profiles

Our review of the tolerance aspects of most of the nab-paclitaxel experiments was permissible. In randomised trials of GeparSepto and ETNA, the condition of toxicity of nab-paclitaxel and paclitaxel in the preoperative context was compared using data. Finally, a total of 1,878 cases were considered in the safety analysis with the stats of all adverse events, including events worse than value 3 [Table 1].

Hematologic toxicity like neutropaenia and leukopenia and an elevation in levels of alanine aminotransferase and aspartate aminotransferase were comparable in both sections but nab-paclitaxel group experienced elevated levels of alanine aminotransferase, and aspartate aminotransferase as compared to those encountered in paclitaxel group. Peripheral sensory neuropathy happens more in the nab-paclitaxel group compared to the paclitaxel group (OR = 2.090, 95 percent CI 1.016-4.302, p = 0.045) and the consequences are unfavourable with regards to haematology in the nab-paclitaxel and paclitaxel group (OR = 2.090, 95 percent CI 1.016-4.302, p The peripheral sensory neuropathy value 3 was feasted three times more among the cases taking nab-paclitaxel (OR = 3.766, 95 percent CI 2.324-6.100, p 0.001). Although the paclitaxel group was already treated before, hypersensitivity to paclitaxel and not to nab-paclitaxel is a possibility at any stage and no exception happens at stage 3-4. The other haematological symptoms including nausea, vomiting, fatigue, and diarrhoea were the same at any given moment between the two groups during the study.

DISCUSSION

This systematic review and meta-analysis demonstrate that nab-paclitaxel is a good cytotoxic agent in neoadjuvant chemotherapy in large cases with HER2+ particularly in aggressive subtypes. In

addition, the first explored meta-analysis of the randomized clinical trial of HER2 + neoadjuvant experience with nabpaclitaxel demonstrated its significant effect on increasing the degree of the pathologic response neurobyotic to 15-30%, which is considerably more than the traditional doses with the generally accepted safety rates of 4-53 percent, with 32 as the higher percentage. There are high levels of pathologic response (ypT0 / N0, 19.8%) with combined analysis of seven potential clinical studies with neoadjuvant anthracycline with standard taxane chemotherapy by the German Breast Group. [13]. More so, early response of nab-paclitaxel among neoadjuvant setting was promising. The clinical response rate was 69.4 percent, in the ETNA test, after the first four cycles of single agent of neoadjuvant nab-paclitaxel, although they did not meet the statistical significance, even though there was an increased level of pathologic response rate with nab-paclitaxel. The first nab-paclitaxel treatment led to a substantial level of tumour necrosis (24 percent) seen in the WSG-ADAPT TN study after biopsy at week three, and this may assist in predicting the amount of pathologic response.

Also, more severe complications cases (61 percent, 95 percent CI 47-74 percent) and TNBC (41 percent) -95 CI 38-45 percent) seem to be gaining more of the pathologic response than any other kind of HER2+. L Lower levels of pathologic response occur in HR+ / HER2 (14 percent 95 percent CI 11-17) cases. The probability of pathologic response was lower in cases treated with neoadjuvant nab-paclitaxel compared to normal, normal dose, or beyond taxane (OR = 1.383, 95 percent CI 1.141-1.676, $p < 0.001$). In a GeparSepto trial, nab-paclitaxel used to treat TNBC almost doubled pathologic response rates achieved by paclitaxel. Tumour response was also good in the cases with TNBC that were first-line treated with nab-paclitaxel in metastatic conditions [15]. Nabpaclitaxel can be a tax-based treatment of TNBC cases in therapy because of the absence of efficient methods to enhance the outcomes, with additional studies being required.

Biomarker guesswork plays an essential role in the pursuit of anti-cancer drugs to ensure the maximum returns of the planned treatment. But there is still no restricted group of cases with the highest probability of using neoadjuvant and paclitaxel treatment. SPARC is an albumin glycoprotein which is a calcium-binding protein which promotes tissue healing [16]. The increase in SPARC in HER2 + cells and stroma might increase its albumin binding, so it should serve as an expected marker of nab-paclitaxel [17]. The benefit of neoadjuvant nab-paclitaxel in SPARC overexpressing subgroup was no longer so different in the SPRC-ve one in GeparSepto study. The information in the metastatic setting could also not reveal a connection between SPARC and nabpaclitaxel efficacy. To come up with predictive indicators of nab-paclitaxel therapy, more data on the major studies that will continue to be required.

CONCLUSION

The above-mentioned meta-analysis points to the potential of nab-paclitaxel as a neoadjuvant agent used to treat HER2+ breast cancer, particularly a heavily aggressive subtype (triple-negative breast cancer, TNBC). Nab-paclitaxel is associated with substantial enhancement of the pathologic response rates, and especially significant clinical outcomes improvement as compared to the traditional paclitaxel treatment. The current systematic review showed that the nab-paclitaxel is used in obtaining the higher pathologic response (ypT0/N0) rates in some HER2+ populations, and the definite advantage is associated with TNBC cases. Nevertheless, nab-paclitaxel has better safety, which is compared to lesser tumor responses and tolerability, although the safety profile should be keenly considered with increased rates of sensory neuropathy, especially at higher doses. Although it has such benefits, there still is a need to conduct more randomized controlled trials to prove conclusively its utility against traditional taxanes, and to determine its use in other patient subgroups, and to determine how it can be used synergistically alongside other drugs. Also, biomarkers such as SPARC that can potentially contribute to increasing the specificity of nab-paclitaxel should be studied further in order to determine the set of the most predictive markers that will allow selecting patients. Future clinical studies can be directed to further define nab- paclitaxel application in treatment through identification of most receptive population, optimizing its regimen and reducing adverse effects. On the whole, nab-paclitaxel emerges as a possible better alternative to neoadjuvant treatment of HER2+

breast cancer, particularly those that are of high-risk/metastatic phenotype, and could form part of a strategy that is evolving in trying to achieve a better outcome in the treatment of breast cancer.

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