

Treatment with nanosomal paclitaxel lipid suspension *versus* conventional paclitaxel in metastatic breast cancer patients – a multicenter, randomized, comparative, phase II/III clinical study

Chiradoni Thungappa Satheesh^{ID}, Rakesh Taran, Jitendra Kumar Singh, Shanti Prakash Shrivastav, Nikunj K. Vithalani, Kalyan Kusum Mukherjee, Rajnish Vasant Nagarkar, Tanveer Maksud, Ajay Omprakash Mehta, Krishnan Srinivasan, Mummaneni Vikranth, Satish Ramkrishna Sonawane, Ateeq Ahmad, Saifuddin Sheikh, Shoukath M. Ali, Ronak Patel, Mahesh Paithankar, Lav Patel, Anil Rajani^{ID}, Deepak Bunger, Alok Chaturvedi and Imran Ahmad^{ID}

Abstract

Background: A novel nanosomal paclitaxel lipid suspension (NPLS), free from Cremophor EL (CrEL) and ethanol, was developed to address the solvent-related toxicities associated with conventional paclitaxel formulation.

Objective: To evaluate the efficacy and safety of NPLS *versus* CrEL-based paclitaxel (conventional paclitaxel) in patients with metastatic breast cancer (MBC).

Design: A prospective, open-label, randomized, multiple-dose, parallel, phase II/III study.

Methods: Adult (18–65 years) female patients with MBC who had previously failed at least one line of chemotherapy were randomized (2:2:1) to NPLS 175 mg/m² every 3 weeks (Q3W, *n* = 48, arm A), NPLS 80 mg/m² every week (QW, *n* = 45, arm B) without premedication or conventional paclitaxel (Taxol®, manufactured by Bristol-Myers Squibb, Princeton, NJ, USA) 175 mg/m² Q3W (*n* = 27, arm C) with premedication. In the extension study, an additional 54 patients were randomized (2:1) to arm A (*n* = 37) or arm C (*n* = 17).

Results: Pooled data from the primary study and its extension phase included 174 patients. The primary endpoint was the overall response rate (ORR). As per intent-to-treat analysis, ORR was significantly better in the NPLS QW arm as compared to conventional paclitaxel [44.4% (20/45) *versus* 22.7% (10/44), (*p* = 0.04)]. An improvement in ORR with NPLS Q3W *versus* conventional paclitaxel arm [29.4% (25/85) *versus* 22.7% (10/44)] (*p* = 0.53) was observed. Disease control rates observed were improved with NPLS Q3W *versus* conventional paclitaxel Q3W (77.7% *versus* 72.7%, *p* = 0.66) and with NPLS QW *versus* conventional paclitaxel Q3W (84.4% *versus* 72.7%, *p* = 0.20), although not significant. A lower incidence of grade III/IV peripheral sensory neuropathy, vomiting, and dyspnea was reported with NPLS Q3W *versus* conventional paclitaxel Q3W arms.

Conclusion: NPLS demonstrated an improved tumor response rate and a favorable safety profile *versus* conventional paclitaxel. NPLS 80 mg/m² QW demonstrated a significantly better response *versus* conventional paclitaxel 175 mg/m² Q3W.

Trial registration: Clinical Trial Registry-India (CTRI), CTRI/2010/091/001344 Registered on: 18 October 2010 (<https://ctri.nic.in/Clinicaltrials/pmaindet2.php?EncHid=MjEzNQ==&Enc=&userName=CTRI/2010/091/001344>), CTRI/2015/07/006062 Registered on: 31 July 2015 (<https://ctri.nic.in/Clinicaltrials/pmaindet2.php?EncHid=MTE2Mjc=&Enc=&userName=CTRI/2015/07/006062>)

Ther Adv Med Oncol

2024, Vol. 16: 1–12

DOI: 10.1177/
17588359241236442

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Correspondence to:

Imran Ahmad
Jina Pharmaceuticals Inc.,
28100 N Ashley Circle,
Suite 103, Libertyville, IL
60048, USA
imran@jinapharma.com

Chiradoni Thungappa Satheesh
Sri Venkateshwara
Hospital, Bangalore,
Karnataka, India

Rakesh Taran
Convenient Hospital Ltd,
CHL-Hospital and CHL-
CBCC Cancer Center,
Indore, Madhya Pradesh,
India

Jitendra Kumar Singh
Mahavir Cancer Sansthan,
Patna, Bihar, India

Shanti Prakash Shrivastav
Kiran Multi Super
Specialty Hospital and
Research Centre, Surat,
Gujarat, India

Nikunj K. Vithalani
Unique Hospital
Multispecialty and
Research Institute, Surat,
Gujarat, India

Kalyan Kusum Mukherjee
Chittaranjan National
Cancer Institute, Kolkata,
West Bengal, India

Rajnish Vasant Nagarkar
Curie Manavata
Cancer Centre, Nashik,
Maharashtra, India

Tanveer Maksud
Bharat Cancer Hospital
and Research Institute,
Surat, Gujarat, India

Ajay Omprakash Mehta
Central India Cancer
Research Institute,
Nagpur, Maharashtra,
India

Krishnan Srinivasan
Dr. Rai Memorial Medical
Centre, Chennai, Tamil
Nadu, India

Mummaneni Vikranth
City Cancer Center,
Vijayawada, Andhra
Pradesh, India

Satish Ramkrishna Sonawane
Anandrishiji Hospital and Medical Research Centre, Ahmednagar, Maharashtra, India

Ateeq Ahmad Saifuddin Sheikh Shoukath M. Ali
Jina Pharmaceuticals, Libertyville, IL, USA

Ronak Patel
Lambda Therapeutic Research Limited, Ahmedabad, Gujarat, India

Mahesh Paithankar Lav Patel

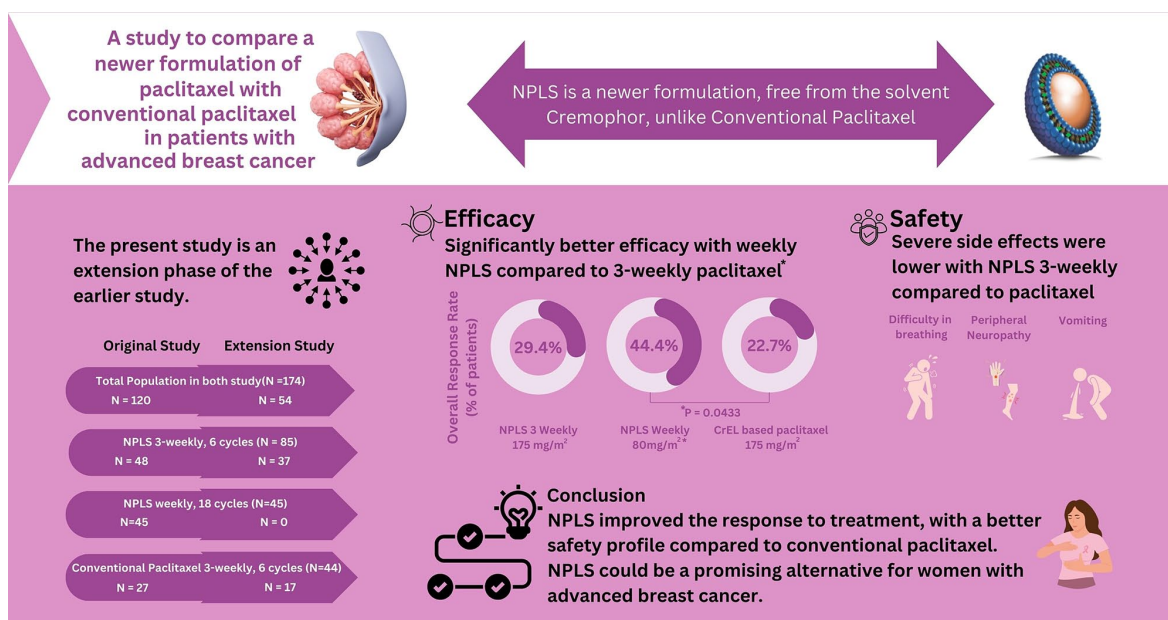
Anil Rajani

Deepak Bunger

Alok Chaturvedi
Intas Pharmaceuticals Ltd, Ahmedabad, Gujarat, India

Jitendra Kumar Singh is currently affiliated to S. S. Hospital and Research Institute, Patna, Bihar, India

Graphical abstract



Plain language summary

Role of nanosomal paclitaxel lipid suspension (NPLS) in the treatment of patients with metastatic breast cancer (MBC)

Why was the study done?

Paclitaxel is a commonly used drug for the treatment of breast cancer. Conventional formulation of paclitaxel is known to cause side effects like injection site reactions. A newer formulation named NPLS was developed to overcome the limitations of the conventional paclitaxel. The current study was done to compare the safety and effectiveness of NPLS and conventional paclitaxel in patients with advanced breast cancer.

What did the researchers do?

The research team conducted a large study in multiple hospitals across India, involving women with advanced breast cancer who had experienced treatment failure with previous chemotherapy. A total of 174 patients were randomly assigned to receive either of the three treatment schedules: (1) NPLS every 3 weeks, (2) NPLS every week, (3) conventional paclitaxel every 3 weeks.

What did the researchers find?

The results showed that NPLS, in a weekly schedule, led to better tumor response rates compared to conventional paclitaxel given every 3 weeks. Additionally, NPLS demonstrated a favorable safety profile, as compared to conventional paclitaxel.

What do the findings mean?

These findings suggest that NPLS could be a promising alternative for women with advanced breast cancer. NPLS improved the response to treatment, with a better safety profile compared to conventional paclitaxel.

Keywords: breast cancer, metastatic, nanosomal paclitaxel lipid suspension, NPLS, PacliAqualip, paclitaxel

Received: 20 July 2023; revised manuscript accepted: 13 February 2024.

Introduction

In the last three decades, breast cancer has moved from fourth to first place in the category of most common cancers.¹ Globally, breast cancer is the most common cancer with an estimated 11.7% of all new cancer cases and a mortality rate of 6.9% as reported in the GLOBOCAN 2020 data.² In India, breast cancer is the most common cancer accounting for 13.5% (178,361) cases of all cancers in 2020.³ The mortality rate of breast cancer in India is highest among other cancers at 10.6%,³ which is attributed to a late diagnosis of disease at locally advanced or metastatic stage.⁴

Metastatic breast cancer (MBC) is incurable and its treatment is directed toward symptom palliation and improving the patient's survival.⁵ Paclitaxel is a preferred chemotherapeutic agent for the treatment of recurrent, unresectable, or stage IV metastatic disease.⁶ Paclitaxel is a highly hydrophobic molecule and hence, in the conventional commercial formulation, a combination of polyethoxylated castor oil [Cremophor EL (CrEL)] and ethanol is used as a vehicle.^{7,8} Studies have indicated that CrEL is an active solvent with biological activities and is known to be associated with toxicities such as severe anaphylactoid hypersensitivity reactions despite corticosteroid premedication; and prolonged, sometimes irreversible, peripheral neuropathy.⁹ Furthermore, CrEL entraps the paclitaxel in plasma through micelle formation leading to a nonlinear pharmacokinetics and thus, causing increased drug levels, decreased drug elimination, and, in turn, diminishing the dose-dependent anticancer effects.^{8,10} Researchers have indicated a need for alternative paclitaxel formulations that are devoid of CrEL to minimize these toxicities.⁹

A novel nanosomal paclitaxel lipid suspension (NPLS, PacliAqualip, manufactured by Intas Pharmaceuticals Ltd., Ahmedabad, India), devoid of CrEL and ethanol, was developed using lipid excipients, Generally Recognized As Safe (GRAS) by the United States Food and Drug Administration (USFDA), to overcome solvent-related toxicity challenges with conventional paclitaxel.^{11,12} NPLS has shown a relatively higher response rate *versus* conventional paclitaxel in the treatment of patients with MBC in a phase II/III study. The initial findings of this study demonstrated a better safety and efficacy [higher overall response rate (ORR) and disease control rate (DCR)] of 3-weekly and weekly NPLS *versus* conventional paclitaxel. There were no severe

hypersensitivity reactions with NPLS, despite the absence of premedication.^{11,12} The current report presents the result of an extension study with updated data from 174 patients (main study: $n = 120$; extended study: $n = 54$).

Methods

This prospective, open-label, randomized, multiple-dose, parallel, phase II/III study enrolled patients from November 2010 to January 2017 (extension study: October 2015–January 2017) and was conducted at 14 sites across India. The study protocol and related documents were reviewed and approved by the institutional review boards or independent ethics committees. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and in accordance with the International Conference on Harmonization's Good Clinical Practice (ICH-GCP) guidelines, applicable regulatory requirements, and compliance with the protocol. All participants provided written informed consent form to participate in the study. The reporting of our study adhered rigorously to the guidelines set forth by Equator Network, following the CONSORT statement (Supplemental Material), which ensures transparency and completeness in reporting our research.

Patient population

Nonpregnant, non-lactating females aged between 18 and 65 years with histologically or cytologically confirmed measurable MBC, who had failed previous combination chemotherapy or relapse within 6 months of adjuvant chemotherapy, and who had an expected survival of more than 6 months were eligible for participation. Patients were included if they had at least one measurable lesion as per the Response Evaluation Criteria in Solid Tumors (RECIST) criteria (version 1.1),¹³ Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 , left ventricular ejection fraction $\geq 50\%$, no previous radiotherapy to $>25\%$ of marrow-containing bones, and who had completed previous chemotherapy or radiotherapy 4 weeks prior to study start. Patients were excluded from participation if they had preexisting motor or sensory neurotoxicity of \geq grade 2 according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), brain metastasis, carcinomatous meningitis or a clinically serious illness,

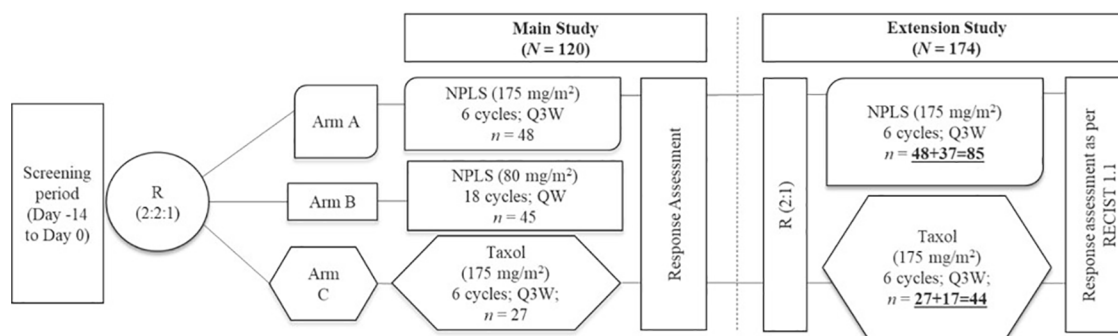


Figure 1. Study design.

NPLS, nanosomal paclitaxel lipid suspension; QW, every week; Q3W, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.

history of hypersensitivity reactions to drugs formulated with CrEL, previous exposure to a taxane injection, or a history of cardiac disease with New York Heart Association class ≥ 2 .

Treatment

In the main study ($n=120$), patients were randomized (2:2:1) to NPLS 175 mg/m² every 3 weeks (Q3W) for a maximum of 6 cycles ($n=48$, arm A), NPLS 80 mg/m² every week (QW) for a maximum of 18 cycles ($n=45$, arm B), or conventional paclitaxel (Taxol®) 175 mg/m² Q3W for a maximum of 6 cycles ($n=27$, arm C). The NPLS 175 mg/m² and conventional paclitaxel 175 mg/m² were administered as an intravenous infusion for 3 h (+30 min), whereas NPLS 80 mg/m² was administered as an intravenous infusion for 1 h (+10 min). NPLS was administered without premedication with corticosteroids and antihistamines, whereas conventional paclitaxel was administered with premedication. The prophylactic granulocyte colony-stimulating factors were administered as per institutional practice. A reduction in treatment dose was allowed according to the package insert or investigator's discretion.

Study design and sample size

At the screening visit, patients enrolling in the study were assigned a unique patient identification number according to the site. This number was serially allocated as per the chronological sequence of patients entering the trial at each site and it also incorporated the site identity. The randomization process was simple, with a block size of 3 (2:1 treatment allocation). For a comparison of two independent binomial proportions using

Pearson's chi-square statistic with a normal approximation with a one-sided significance level of 0.0294, a total of 108 completers, assuming an allocation ratio of 2:1 (72:36 in arm A:arm C) was expected to achieve a power of $\geq 80\%$ when the proportions were 20.8% and 36.4% and the non-inferiority margin was -10% .

In the main study, there were a total of 69 completers (44 and 25 completers in arms A and C respectively). Hence, as per guidance from the Drugs Controller General of India, an additional 54 patients were enrolled in a 2:1 ratio (36 and 18 patients) in arms A and C, respectively, in the extension study to achieve a power of 80%, a non-inferiority limit of 10%, and an α -error of 5% for analysis. However, of these additional 54 patients, 37 patients in arm A and 17 patients in arm B were enrolled due to site-specific randomization and it did not have any significant impact on the objectives of the study (Figure 1).

Study assessments

The primary study endpoint was ORR, defined as the proportion of patients whose best overall response was complete response (CR) or partial response (PR) after receiving at least two cycles of study treatment of NPLS or Taxol®. The secondary endpoint was DCR, defined as the proportion of patients with CR, or PR or stable disease (SD) (DCR = CR + PR + SD). The safety variables included adverse events (AEs), laboratory tests, vital signs, physical examination findings, concomitant medications, and electrocardiograms.

The efficacy evaluations were performed after 2, 4, and 6 cycles each in arms A and C, whereas in arm B, these were performed after 6, 12, and 18 cycles.

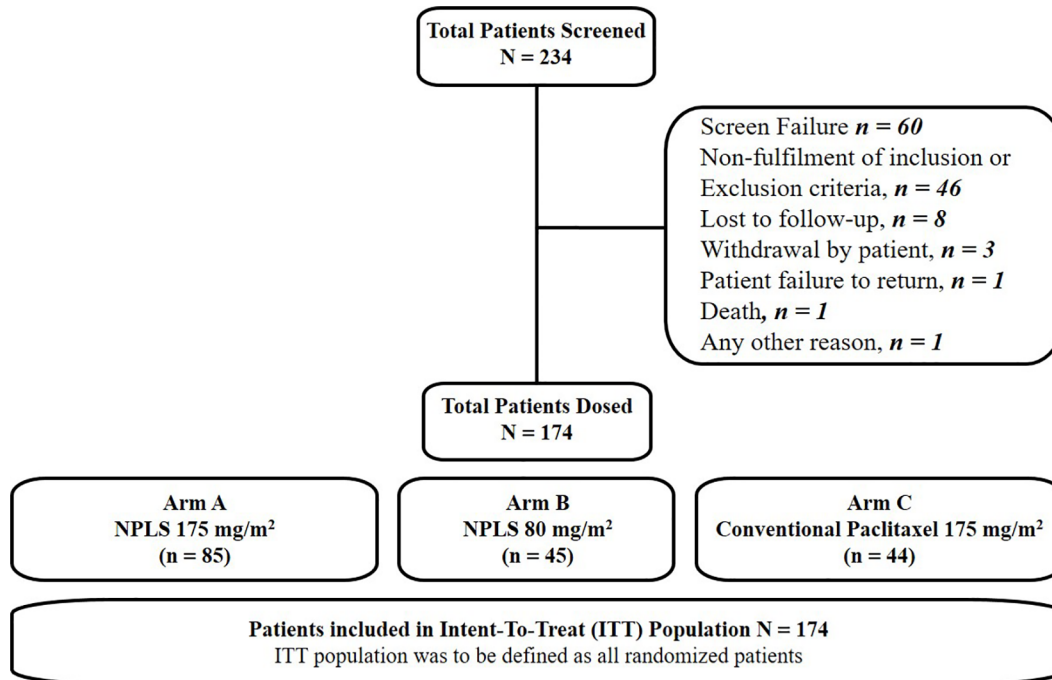


Figure 2. Patient disposition. ITT population included all randomized patients who received at least one dose of study medication.

CT, computed tomography; ITT, intent-to-treat; MRI, magnetic resonance imaging; NPLS, nanosomal paclitaxel lipid suspension.

Treatment response was assessed by an independent radiologist and analyzed using the RECIST version 1.1.¹³ The incidence of AEs documented in the treatment charts was recorded and graded according to the CTCAE criteria version 4.3.¹⁴

Statistical analysis

The statistical analysis was performed on the pooled data of the main study and the extension study. The efficacy population was defined as all patients who were evaluated for a response (computed tomography scan/magnetic resonance imaging) after receiving at least two treatment cycles, with no major protocol violations. The safety assessments were performed on a safety population that included all randomized patients who received at least one dose of study medication. Continuous variables were summarized using summary statistics (number of observations, mean, standard deviation, median, minimum and maximum, etc.) as applicable. Categorical values were summarized by dose group using frequencies and percentages. A point estimate and a two-sided 95% confidence interval (95% CI) were calculated for efficacy endpoints. Fisher's exact test was used to compare the groups for significance. All statistical comparisons were

performed using a two-sided significance level $\alpha=0.05$. The AEs were summarized as frequencies and percentages by type of reactions. The randomization and statistical analyses were performed by a biostatistician using SAS[®] version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Patient disposition and demographics

All patients from the main study were included in the study population and respective analyses without any changes in this extension study. A total of 234 female patients were screened, of whom, 174 (120 from the main study and 54 from the extension study) were randomized to arm A ($n=85$), arm B ($n=45$), and arm C ($n=44$), respectively. Efficacy and safety endpoints were analyzed with data from the intent-to-treat (ITT) population ($n=174$) (Figure 2).

The mean (SD) age of the patients was 48.2 (8.8) years, and the mean body surface area (BSA) was 1.5 (0.2) kg/m². The racial makeup of the study was 100% Asian. The majority (>90%) of the patients had received prior anthracycline-based regimens in the adjuvant or metastatic

Table 1. Demographics and baseline characteristics (safety population, N = 174).

Parameter	NPLS (175 mg/m ²) (N = 85) Arm A	NPLS (80 mg/m ²) (N = 45) Arm B	Conventional paclitaxel (175 mg/m ²) (N = 44) Arm C
Age in years, mean (SD)	48.2 (8.8)	47.5 (9.7)	49.5 (8.3)
Gender, female, n (%)	85 (100)	45 (100)	44 (100)
BSA (m ²), mean (SD)	1.5 (0.2)	1.4 (0.2)	1.5 (0.2)
BMI (kg/m ²)	23.4 (4.8)	22.7 (4.8)	23.9 (4.9)
ECOG performance score, n (%)			
0	26 (30.6)	22 (48.9)	15 (34.1)
1	52 (61.2)	20 (44.4)	23 (52.3)
2	7 (8.2)	3 (6.7)	6 (13.6)
Menopausal status, n (%)			
Pre-menopausal	40 (47.1)	18 (40)	17 (38.6)
Post-menopausal	45 (52.9)	27 (60)	27 (61.4)
Prior chemotherapy regimens in the metastatic setting, n (%)			
0 ^a	45 (52.9)	16 (35.6)	26 (59.1)
1	40 (47.1)	29 (64.4)	18 (40.9)

^aPatients receiving study drugs as first-line therapy in metastatic settings included those who relapsed within 6 months of adjuvant chemotherapy.
BMI, body mass index; BSA, body surface area; ECOG, Eastern Cooperative Oncology Group; NPLS, nanosomal paclitaxel lipid suspension; SD, standard deviation.

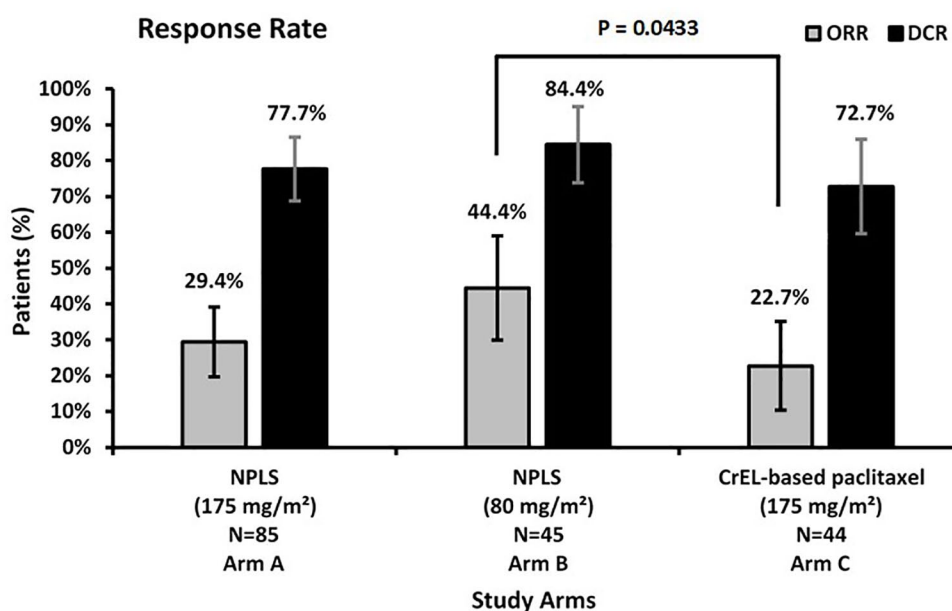


Figure 3. Response rates.
DCR, disease control rate; NPLS, nanosomal paclitaxel lipid suspension; ORR, overall response rate.

Table 2. Response rates (N=174).

Response	NPLS (175 mg/m ²) (N=85) Arm A, n (%)	NPLS (80 mg/m ²) (N=45) Arm B, n (%)	Conventional paclitaxel (175 mg/m ²) (N=44) Arm C, n (%)
CR	3 (3.5)	0 (0)	0 (0)
PR	22 (25.9)	20 (44.4)	10 (22.7)
SD	41 (48.2)	18 (40)	22 (50)
ORR (CR + PR)	25 (29.4)	20 (44.4)	10 (22.7)
DCR (CR + PR + SD)	66 (77.6)	38 (84.4)	32 (72.7)

CR, complete response; DCR, disease control rate; NPLS, nanosomal paclitaxel lipid suspension; ORR, overall response rate; PR, partial response; SD, stable disease.

setting. Overall, the demographic and baseline characteristics were similar among the treatment groups (Table 1).

Efficacy

The ORR was significantly higher for NPLS QW *versus* conventional paclitaxel Q3W (44.4% *versus* 22.7%, $p=0.04$). An improvement in ORR with NPLS Q3W *versus* conventional paclitaxel Q3W was observed (29.4% *versus* 22.7%, $p=0.53$). An improved DCR was observed with NPLS Q3W *versus* conventional paclitaxel Q3W arm (77.7% *versus* 72.7%, $p=0.66$) and NPLS QW *versus* conventional paclitaxel Q3W arm (84.4% *versus* 72.7%, $p=0.20$), although not significantly different. A CR was achieved in three patients in the NPLS Q3W arm, whereas no CR was reported in other treatment arms (Figure 3 and Table 2). A per-protocol analysis was also done for 168 patients with no major protocol violation and with available efficacy data after at least two cycles of chemotherapy. Improved responses in ORR or DCR were observed, although not significant.

Safety

The proportion of patients with at least one AE was not statistically different between the three study arms (72.9% in the 3-weekly NPLS arm, 82.2% in the weekly NPLS arm, and 70.5% in the paclitaxel arm; $p=0.3855$). Table 3 provides the AEs occurring in $\geq 5\%$ of patients in any treatment arm. A general trend toward a lesser incidence of all grade AEs for peripheral sensory neuropathy, diarrhea, vomiting, and anorexia was observed with NPLS *versus* conventional

paclitaxel. A lower incidence of grade III/IV AEs in the NPLS Q3W *versus* conventional paclitaxel Q3W arms in terms of peripheral sensory neuropathy, vomiting, dyspnea, and a higher incidence of neutropenia was observed.

The proportion of patients experiencing serious adverse events (SAEs) was 7.1% ($n=6/85$) for NPLS Q3W, 11.1% ($n=5/45$) for NPLS QW, and 9.1% ($n=4/44$) for conventional paclitaxel Q3W arms ($p=0.6877$). The SAEs in the NPLS Q3W arm were febrile neutropenia, pleural effusion, pyrexia, and dyspnea in one patient each, those in the NPLS QW arm were urinary tract infection, lung infection, pyrexia, food poisoning, and lymphedema in one patient each, and in conventional paclitaxel Q3W arm were dyspnea and vomiting in one patient each.

There were four deaths reported [two patients (2.4%) in the NPLS Q3W arm and two patients (4.5%) in the conventional paclitaxel Q3W arm]. In the NPLS Q3W arm, one death each ($n=2$) was reported due to febrile neutropenia and pyrexia, which were considered by the investigator to be probably and unlikely related to treatment, respectively. In the conventional paclitaxel Q3W arm, one death each ($n=2$) was reported due to respiratory distress and cardio-respiratory failure, both were considered by the investigator to be unlikely related to treatment. Notably, no death was reported in the NPLS QW arm.

Discussion

In this phase II/III study with an extension phase, NPLS, a novel CrEL-free formulation of paclitaxel, in a weekly regimen demonstrated a higher

Table 3. Adverse events occur in $\geq 5\%$ of patients in any treatment arm (N=174).

AEs	NPLS (175 mg/m ²) (N=85) Arm A, n (%)		NPLS (80 mg/m ²) (N=45) Arm B, n (%)		Conventional paclitaxel (175 mg/m ²) (N=44) Arm C, n (%)	
	Grade 1–2	Grade ≥ 3	Grade 1–2	Grade ≥ 3	Grade 1–2	Grade ≥ 3
Alopecia	18 (21)	0	8 (18)	0	9 (20)	0
Anemia	6 (7)	2 (2)	9 (20)	4 (9)	4 (9)	0
Asthenia	11 (13)	0	2 (4)	0	4 (9)	0
Back pain	9 (11)	1 (1)	5 (11)	2 (4)	0	0
Chest discomfort	1 (1)	0	0	0	3 (7)	0
Chills	18 (21)	1 (1)	8 (18)	3 (7)	1 (2)	0
Cough	4 (5)	0	6 (13)	0	3 (7)	0
Decreased appetite	5 (6)	0	0	0	5 (11)	0
Diarrhea	5 (6)	0	4 (9)	0	5 (11)	0
Dyspnea	4 (5)	1 (1)	7 (16)	0	0	1 (2)
Edema peripheral	0	0	4 (9)	0	0	0
Headache	4 (5)	1 (1)	1 (2)	3 (7)	2 (4)	0
Hypertension	2 (2)	0	4 (9)	2 (4)	1 (2)	0
Nausea	6 (7)	0	3 (7)	0	3 (7)	0
Neutropenia	11 (13)	7 (8)	8 (18)	3 (7)	2 (5)	2 (4)
Pain	11 (13)	0	1 (2)	1 (2)	4 (9)	0
Peripheral sensory neuropathy	10 (12)	1 (1)	1 (2)	2 (4)	9 (20)	1 (2)
Pruritus	3 (3)	0	1 (2)	0	3 (7)	0
Pyrexia	14 (16)	1 (1)	4 (9)	1 (2)	5 (11)	0
Tachycardia	3 (3)	0	3 (7)	0	0	0
Vomiting	6 (7)	0	5 (11)	0	3 (7)	1 (2)

ORR compared to conventional paclitaxel. NPLS demonstrated an acceptable safety profile as compared with conventional paclitaxel formulation. DCR data were comparable between the three study arms. The ORR and DCR results presented here are consistent with the previous publication of the aforementioned parameters from this trial.^{11,12} NPLS was well tolerated overall and could be administered without corticosteroid and antihistaminic premedication in patients with MBC.

NPLS was developed using ‘NanoAqualip’ technology.^{15,16} Nano-sized (~100nm) drug particles formulated with this technology may facilitate penetration of the drug to the tumor vasculature, and due to the decreased lymphatic drainage in the tumor, the retention and extravasation of NPLS in the tumor bed may increase and exert enhanced permeability and retention (EPR) effects possibly leading to enhanced antitumor activity.^{17,18} Consistent with this hypothesis,

NPLS in the current study demonstrated an improved activity in terms of response rates.

The dose regimens of NPLS 175 mg/m² Q3W and 80 mg/m² QW used in the current study were in line with the prescribing information, treatment guidelines, and clinical practice.^{6,7,19} Paclitaxel is approved at a dose of 175 mg/m² Q3W for the management of MBC⁷ and reported an ORR of 29% in the landmark phase III trial by Siedman *et al.* ($n=735$).²⁰ Another study by Winer *et al.* ($n=472$) reported an ORR of 23% with a paclitaxel 175 mg/m² Q3W regimen.²¹ In our study, the conventional paclitaxel at 175 mg/m² Q3W regimen reported an ORR of 22.7% in line with previous reports, whereas the NPLS 175 mg/m² Q3W regimen reported an ORR of 29.4%.

Paclitaxel in a weekly regimen decreases myelosuppression and toxicity but at the same time maintains a higher dose intensity for improved efficacy outcomes as compared with standard Q3W regimens.²² The efficacy and safety of weekly paclitaxel in MBC have been reported in several studies with an ORR ranging from 30% to 50%.^{19,23–26} In the current study, the NPLS 80 mg/m² QW arm demonstrated a significantly better ORR as compared with conventional paclitaxel 175 mg/m² Q3W arm (44.4% *versus* 22.7%, $p=0.0433$).

Another solvent-free formulation approved for MBC is nab-paclitaxel. In the phase III trial of nab-paclitaxel at a 3-weekly dose of 260 mg/m², it demonstrated an ORR of 33% *versus* 19% with conventional paclitaxel at a 3-weekly dose of 175 mg/m².⁸ Conceptually, both NPLS and nab-paclitaxel are solvent-free formulations and hence these can overcome the shortcomings of conventional paclitaxel – namely, hypersensitivity, requirement of pre-medications like steroids, non-linear pharmacokinetics, etc. although both formulations have different dosing recommendations. While NPLS is dosed at an equivalent dose of conventional paclitaxel at the 3-weekly regimen of 175 mg/m², nab-paclitaxel is dosed at ~50% higher dose at the 3-weekly regimen of 260 mg/m².²⁷ A head-to-head study between NPLS and nab-paclitaxel in future can provide further data about the differences between efficacy and safety of these novel formulations.

NPLS is approved in India for the treatment of MBC, metastatic ovarian cancer, metastatic non-small-cell lung cancer, and acquired immune deficiency syndrome-related Kaposi's sarcoma.²⁸ An

Indian expert panel (funded by Intas Pharmaceuticals Limited) opined that novel CrEL-free formulations of paclitaxel like NPLS add value in the management of MBC and has recommended their usage in MBC patients who are at risk of hypersensitivity, diabetes, or patients with conditions that preclude the use of corticosteroids.²⁹

While our investigation revealed encouraging findings concerning the effectiveness and safety of NPLS in treating MBC, it is crucial to acknowledge certain limitations that merit consideration. These limitations include a short follow-up duration, age restriction of up to 65 years of age, lack of survival outcomes, a single country setting, and the absence of a weekly conventional paclitaxel arm as control, which may impact the generalizability of the study findings. Future studies with a larger sample size and an extended follow-up period to capture long-term outcomes and to assess potential late-onset AEs are warranted.

Conclusion

NPLS administered at a dose of 175 mg/m² Q3W or 80 mg/m² QW demonstrated a relatively improved tumor response *versus* conventional paclitaxel 175 mg/m² administered Q3W in patients with MBC. NPLS 80 mg/m² QW demonstrated a significantly better ORR *versus* conventional paclitaxel 175 mg/m² Q3W. Overall, NPLS was well-tolerated without any significant safety concerns. In patients with MBC, NPLS may be an alternative treatment option as it precludes the need for premedication.

Declarations

Disclosure

Dr Ateeq Ahmad, Dr Saifuddin Sheikh, Dr Shoukath M Ali, and Dr Imran Ahmad are employees of Jina Pharmaceuticals, Libertyville, IL, USA. Mr Ronak Patel is an employee of Lambda Therapeutic Research Limited, Ahmedabad India. Mr Mahesh Paithankar, Dr Lav Patel, Dr Anil Rajani, Dr Deepak Bunker, and Dr Alok Chaturvedi are employees of Intas Pharmaceuticals Limited, Ahmedabad, India.

Previous presentation

The study data were presented as a poster at the European Society of Medical Oncology (ESMO) Congress, held in Paris, from 9 to 13 September 2022.

Ethics approval and consent to participate

Ethical approval for this study was obtained from the Institutional Ethics Committee (IEC) of the respective trial sites. This study is registered on Clinical Trial Registry-India (CTRI) vide registration numbers CTRI/2010/091/001344 (registered on 18 October 2010) and CTRI/2015/07/006062 (registered on 31 July 2015). The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and in accordance with the International Conference on Harmonization's Good Clinical Practice (ICH-GCP) guidelines, applicable regulatory requirements, and in compliance with the protocol. All participants provided a written informed consent form to participate in the study.

Consent for publication

Consent for publication was obtained from all authors, participants, or legally authorized representatives involved in this study.

Author contributions

Chiradoni Thungappa Sathesh: Investigation; Project administration; Resources; Supervision.

Rakesh Taran: Investigation; Project administration; Resources; Supervision.

Jitendra Kumar Singh: Investigation; Project administration; Resources; Supervision.

Shanti Prakash Shrivastav: Investigation; Project administration; Resources; Supervision.

Nikunj K. Vithalani: Investigation; Project administration; Resources; Supervision.

Kalyan Kusum Mukherjee: Investigation; Project administration; Resources; Supervision.

Rajnish Vasant Nagarkar: Investigation; Project administration; Resources; Supervision.

Tanveer Maksud: Investigation; Project administration; Resources; Supervision.

Ajay Omprakash Mehta: Investigation; Project administration; Resources; Supervision.

Krishnan Srinivasan: Investigation; Project administration; Resources; Supervision.

Mummaneni Vikranth: Investigation; Project administration; Resources; Supervision.

Satish Ramkrishna Sonawane: Investigation; Project administration; Resources; Supervision.

Ateeq Ahmad: Conceptualization; Resources; Visualization; Writing – review & editing.

Saifuddin Sheikh: Conceptualization; Resources; Visualization; Writing – review & editing.

Shoukath M. Ali: Conceptualization; Resources; Visualization; Writing – review & editing.

Ronak Patel: Data curation; Formal analysis; Software; Validation.

Mahesh Paithankar: Conceptualization; Methodology; Validation; Visualization.

Lav Patel: Validation; Visualization; Writing – review & editing.

Anil Rajani: Validation; Visualization; Writing – review & editing.

Deepak Bunger: Validation; Visualization; Writing – review & editing.

Alok Chaturvedi: Methodology; Supervision; Validation; Visualization; Writing – review & editing.

Imran Ahmad: Conceptualization; Data curation; Project administration; Supervision; Writing – review & editing.

Acknowledgements

The authors would like to thank Dr Mehul R. Chorawala and Ms. Sakshi Srivastava (Intas Pharmaceuticals Limited, Ahmedabad, India) for providing scientific writing assistance and follow-up with Editorial office of Journal. The authors are also grateful to Chintan Bodiwala and the clinical data management and biostatistics department of Lambda Therapeutic Research Ltd, Ahmedabad, India for statistical analysis.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was funded by Intas Pharmaceuticals Ltd, Ahmedabad, Gujarat, India.

Competing interests


Dr Ateeq Ahmad, Dr Saifuddin Sheikh, Dr Shoukath M Ali, and Dr Imran Ahmad are employees of Jina Pharmaceuticals, Libertyville, IL, USA. Mr Ronak Patel is an employee of Lambda Therapeutic Research Limited, Ahmedabad India. Mr Mahesh Paithankar, Dr Lav Patel, Dr Anil Rajani, Dr Deepak Bunger,


and Dr Alok Chaturvedi are employees of Intas Pharmaceuticals Limited, Ahmedabad, India.

Availability of data and materials

The data that support the findings of this research are not publicly available due to institutional restrictions.

ORCID iDs

Chiradoni Thungappa Satheesh  <https://orcid.org/0000-0003-0822-7747>

Anil Rajani  <https://orcid.org/0000-0002-2477-9499>

Imran Ahmad  <https://orcid.org/0000-0001-6383-0093>

Supplemental material

Supplemental material for this article is available online.

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