

Research Article

Efficacy and Safety of Nab-Paclitaxel in the Treatment of Metastatic Breast Cancer: A Real-Life Experience

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Abstract

Aims: Evaluate safety and efficacy of nab-paclitaxel in pre-treated metastatic breast cancer (MBC) patients in a real-life setting.

Patients and Methods: This single centre perspective non-comparative trial evaluated MBC patients treated with nab-paclitaxel. Primary endpoint was safety. Secondary endpoints were: overall response rate, progression free survival (PFS) and overall survival (OS).

Results: 31 patients were enrolled. The main toxicities were fatigue (78%), pain (52%), neutropenia (42%) and febrile neutropenia (36%). The median OS was 10.2 months and median PFS was 4.5 months. A partial response was observed in 19.3% of patients and a stable disease in 38.7% of cases; the clinical benefit rate was 58%.

Conclusions: Nab-paclitaxel represents a valid therapeutic option for the treatment of highly pre-treated MBC patients

Keywords: Breast cancer; Efficacy & Safety; Metastatic breast cancer; Nab-paclitaxel; Real-life

1. Introduction

Metastatic breast cancer (MBC) is a widely spread cancer in women worldwide. According to AIRTUM 2016, about 50,000 new cases of MBC were diagnosed in Italy. Breast cancer is the mostly diagnosed cancer (excluding skin carcinoma) in Italian women (30% of tumours). Furthermore, in 2013 the breast cancer was the first cause of cancer-associated death in women (11,939 deaths). However, due to the development of new systemic treatments, including more and more effective combination of chemotherapy and target drugs, the 5-years survival of women with breast cancer is 85.5% in Italy; this rate is higher than both European median rate (81,8%) and North European countries one (84.7%) [1]. Nevertheless, the objectives of treatment in the metastatic setting are still palliative and aimed at controlling symptoms, improving and maintaining quality of life (QoL), and prolonging survival, with a careful balance between efficacy and safety [2].

According to the most recently published International and National Guidelines, taxanes (paclitaxel and docetaxel) are the more effective cytotoxic drugs in MBC, both in monotherapy and in combination with other agents [3-6]. Despite this, it has been shown that the synthetic solvents included in the taxanes formulations (because of drugs' hydrophobicity) can increase some toxicities, such as hypersensitivity reactions and peripheral neuropathy [7]. Besides, apremedication with corticosteroids and antihistamines is requested, increasing the risk of additional adverse events [2]. Nab-paclitaxel is a colloidal suspension of paclitaxel and human albumin in nanoparticles without chemical solvents. This drug uses the natural properties of

albumin in order to increase the drug concentration in the tumoral environment [8-9] Nab-paclitaxel allows the safe infusion of significantly higher doses of paclitaxel than standard paclitaxel in a shorter infusion time (30 min vs 3 hours) without the need of a premedication. Nab-paclitaxel was developed in order to improve the well-known anticancer activity of standard paclitaxel in terms of higher efficacy and better tolerability [7].

The objective of this study was to evaluate the safety and the efficacy of nab-paclitaxel in pre-treated MBC patients in a real-life setting.

2. Patients and Methods

This single centre perspective open non-comparative trial was performed at the Mediterranean Institute of Oncology, Viagrande (CT), Italy, on patients with metastatic breast cancer treated with nab-paclitaxel (Abraxane®) in different lines of treatment. All the data were stored in a database and analyzed. The main patient inclusion criteria were the following: adult patients (≥ 18 years) with previously treated and histologically and cytologically confirmed metastatic breast cancer; Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 ; at least one target lesion measurable according to RECIST (Response Evaluation Criteria in Solid Tumors) criteria; adequate bone marrow, liver and renal function; no other concomitant malignancy; life expectancy of at least 3 months. All the patients were treated with nab-paclitaxel as a single agent at the dose of 260 mg/m² as a 30 min intravenous infusion on day 1 of each 3-weeks cycle, until disease progression or unacceptable toxicity. The primary endpoint of this study was the drug safety in the clinical practice (i.e., in no selected patients such as those enrolled in clinical trials). The secondary endpoint was to evaluate our experience on the efficacy of nab-paclitaxel in patients with metastatic

breast cancer in terms of objective overall response rate (ORR), progression free survival (PFS) and overall survival (OS).

This study has been conducted according to the Declaration of Helsinki; all patients provided a written informed consent before undergoing any study-specific procedure.

3. Results

A total of 31 patients were evaluated at the Mediterranean Institute of Oncology from January 1st 2012 to March 1st 2015. Table 1 shows the clinical characteristics of the patients. The mean age was 58.1 years (range: 36 - 77) and the ECOG performance status was 0–1 in 77.4% of cases. 83.7% of patients had an estrogen receptor (ER) positive tumour and 71% of patients a progesteron receptor (PgR) positive cancer. As previously showed, all the patients had a metastatic disease: 3/31 patients with bone metastases only, 8/31 with visceral metastases (lung, liver, brain, adrenal glands and skin) and 20/31 with bone and visceral metastases.

Patients received the study drug for the metastatic disease in different lines of treatment: 1 in first line, 8 in second line, 6 in third line, 10 in fourth line, 5 in fifth line and 1 in seventh line, with a median of 4 lines. The median number of cycles was 5 (range:1-12); 18 patients (57.6%) received at least 5 cycles of therapy. Safety was evaluated in each patient. Fatigue was the most common observed toxicity (Table 2), occurring in approximately 78% of patients. Other adverse events reported during the study were: pain (52%), neutropenia (42%), febrile neutropenia (36%), peripheral neuropathy (19%), anemia (10%) and vomitus (3%). No Grade 4 adverse events occurred during the study. Patients treated with nab-paclitaxel had a median OS of 10.2 months and median PFS of 4.5 months. A partial response (PR) was observed in 19.3% of patients and a stable disease (SD) in 38.7% of patients; the clinical benefit rate (CBR) was 58% (Table 3). Table 4 shows the clinical efficacy in accordance with biomolecular expression. As expected, a higher treatment efficacy was observed in luminal A (PR=75%) and B (PR=40,9%) breast cancers.

	N	%
Total number of patients	31	100
Meanage (year, range)	58.1 (36- 77)	
ECOG performance status		
0	7	22.6
1	17	54.8
2	7	22.6
Tumour characteristics		
Luminal A	4	12.8
Luminal B	22	71
Triple negative	2	6.5
HER2 like	3	9.7
Metastatic sites		
Bone	3	9.7

Visceral	8	25.8
Bone/visceral	20	64.5
Previous treatments		
Hormonal	19	61.4
Anthracyclines	22	71
Taxanes	16	51.6
Previous chemotherapy lines		
1	1	3.2
2	8	25.8
3	6	19.4
4	10	32.2
> 4	6	19.4

Table 1: Demographic and clinical characteristics of patients.

Adverse events (%)	G1	G2	G3	Total
Haematologic				
Neutropenia	0	26%	16%	42%
Anemia	3%	7%	0	10%
Febrile neutropenia	0	26%	10%	36%
Non haematologic				
Peripheral neuropathy	0	19%	0	19%
Fatigue	7%	26%	45%	78%
Vomiting	0	3%	0	3%
Pain	3%	39%	10%	52%
Hypersensitivity	3%	0	0	3%

Table 2: Main toxicities observed during the study.

Median OS (months)	10.2
Median PFS (months)	4.5
ORR (%)	19.3
PR	19.3
SD	38.7
CBR	58

OS=overall survival; PFS=progression free survival; ORR=overall response rate; PR=partial response; SD=stable disease;

CBR=clinical benefit rate

Table 3: Clinical efficacy.

	Luminal A	Luminal B	HER2 like	TN
PR (% , n)	75% (3)	40,9% (9)	0	0
SD (% , n)	25% (1)	45,5% (10)	33,3% (1)	0
PD (% , n)	0	13,6% (3)	66,7% (2)	100% (2)

PR=partial response; SD=stable disease; PD=disease progression; TN, triple negative

Table 4: Clinical efficacy in accordance with biomolecular expression.

4. Discussion

Metastatic breast cancer is considered an incurable disease, despite the availability of effective multidisciplinary therapeutic strategies. In the last decades a significant increase of survival of metastatic patients was observed, mainly due to the availability of more effective drugs and a widespread diffusion of information and prevention [2]. The pivotal trial by Gradishar et al. demonstrated the higher efficacy and the better safety profile of nab-paclitaxel compared to standard paclitaxel in the second line treatment of this patients' population; furthermore, the improved therapeutic index, as well as the lack of the premedication with corticosteroids, needed for standard taxanes, make nab-paclitaxel an important and innovative therapeutic option for the metastatic breast cancer [10].

In our experience of “real life” clinical practice, nab-paclitaxel was used in a limited number of heterogenous patients in order to evaluate its efficacy and safety. In fact, unlike Gradishar trial [10], where the enrolled patients were selected according to standard inclusion criteria (460 taxane naïve patients or treated with an adjuvant taxane more than 12 months before the start of the study), in our case patients were not selected according strict criteria and were usually heavily pre-treated (several chemotherapy lines). Besides, 60% of patients enrolled in the pivotal trial have been treated with at least 6 cycles of nab-paclitaxel and > 90% of patients in second line therapy; in our case, only 40% of patients received more than 6 cycles of chemotherapy and <

30% of patients received nab-paclitaxel in second line (70% of cases > 3rd line and 50% > 4th line). In spite of these significant differences, our median OS and PFS were 10.2 months and 4.5 months respectively, with an impact on the survival and clinical stability of the patients even in the advanced lines of treatment.

Some Italian experiences evaluated the efficacy and safety of nab-paclitaxel in the real-life setting. Palumbo et al. performed a perspective, multicenter trial to assess the activity, safety, and quality of life of nab-paclitaxel 260 mg/m² every 3 weeks in the second line treatment of 52 patients HER2-negative, taxane-pretreated MBC. ORR was 48%, including 13.5% of complete responses, and the clinical benefit rate was 77%. The median PFS was 8.9 months and the median OS had not yet been reached when the article was published [2]. Another single centre perspective open trial evaluated the efficacy and safety of nab-paclitaxel (260 mg/m² every 3 weeks or 125 mg/m² weekly) in 42 patients with taxane pre-treated MBC. The results were the following: ORR 23.8%; median duration of response 7.2 months; median PFS 4.6 months. These data were similar irrespective of the previous chemotherapy lines, metastatic sites, and biomolecular expression. The 12-months OS rate was 53.8% [7]. Finally, the recently published study by Bernardo et al. prospectively collected data of 209 patients with advanced breast cancer treated with a weekly (125 mg/m² for 3/4 weeks of each 4-week cycle, n=92) or with a 3-week schedule (260 mg/m²,

n=117) of nab-paclitaxel; the choice of schedule was at the discretion of the investigator. The median number of cycles was 5.5. ORR was 32.1%, without any significant difference according to schedule, previous paclitaxel exposure, presence of visceral metastases or line of treatment. CBR (complete response plus partial response plus stable disease) was 57.7%. The median time to disease progression (TTP) was 6 months and the median OS 18 months [11]. All together, these Italian real-life data confirm that nab-paclitaxel as single agent is effective, safe and easy to manage in the treatment of pretreated MBC patients.

As already observed in Gradishar trial [10], also in our experience nab-paclitaxel was safe in terms of tolerability and toxicity: no grade 4 adverse event or events leading to the treatment withdrawn were reported. Fatigue was the most commonly reported toxicity (78%); rates of the haematologic events (neutropenia 42% and anemia 10%) and peripheral neuropathy (19%) were lower than those observed in Palumbo and Fabi trials [2,7]. On the contrary, the rates of patients with neutropenia (9.4%) and fatigue (27.4%) reported in Bernardo trial were lower than in our trial, while the peripheral neuropathy rate (29.9%) was higher [11].

5. Conclusion

Based on these real-life results, nab-paclitaxel represents a valid therapeutic option for the treatment of highly pretreated MBC patients. In addition, in patients subjected to extended thyroidectomy a reduction of recurrence rate is documented by virtually all studies and, finally, the psychological burden of the patient and the high medical cost following a cancer recurrence must be also taken in account.

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Conflict of Interest

The authors declare no potential conflicts of interest.

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Ethical Approval

Patients were enrolled at the Mediterranean Institute of Oncology (IOM) (Viagrande, Italy) under an approved Institutional Review Board protocol (project ID code: 1127-02 of 8 November 2011, IOM Institutional Review Board). Written informed consent has been obtained from all patients who agreed to participate to the present study.

References

1. I numero del cancro in Italia; 2016 [The number of cancer in Italy; 2016] Available from: <http://www.registri-tumori.it/cms/it/node/4572>.
2. Palumbo R, Sottotetti F, Trifirò G, et al. Nanoparticle albumin-bound paclitaxel (nab-paclitaxel) as second-line chemotherapy in HER2-negative, taxane-pretreated metastatic breast cancer patients: prospective evaluation of activity, safety, and quality of life, *Drug Des Devel Ther* (2015): 2189-2199.
3. AIOM Guidelines. Neoplasie della mammella 2016. Available from: <https://www.aiom.it/neoplasie-della-mammella-8/>
4. Cardoso F, Costa A, Senkus E, et al. 3rd ESO–ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 3), *Ann Oncol* 28 (2017): 16-33.

5. Partridge AH, Rumble RB, Carey LA, et al. Chemotherapy and Targeted Therapy for Women With Human Epidermal Growth Factor Receptor 2–Negative (or unknown) Advanced Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline, *J Clin Oncol* 32 (2014): 3307-3329.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Breast cancer. Version 3 (2017).
7. Fabi A, Giannarelli D, Malaguti P, et al. Prospective study on nanoparticle albumin-bound paclitaxel in advanced breast cancer: clinical results and biological observations in taxane-pretreated patients, *Drug Des Devel Ther* 9 (2015): 6177-6183.
8. Henderson IC, Bathia V. Nab-paclitaxel for breast cancer: a new formulation with an improved safety profile and greater efficacy, *Expert Rev Anticancer Res* 7 (2007): 919-943.
9. Yardley DA. Nab-Paclitaxel mechanisms of action and delivery, *J Control Release* 170 (2013): 365-372.
10. Gradishar WJ, Tjulandin S, Davidson N, et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer, *J Clin Oncol* 23 (2005): 7794-803.
11. Bernardo A, Palumbo R, Pedersini R, et al. Nab-Paclitaxel in Advanced HER2-negative Breast Cancer Patients: Efficacy and Safety Beyond Clinical Trials, *Clin Breast Cancer* 17 (2017): 433-440.



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