Retrospective Audit on the use of Albumin-Bound Paclitaxel (Nab-Paclitaxel) and its Outcomes in Dubai Hospital

Abstract

**Background:** Albumin-bound paclitaxel (nab-paclitaxel) is a solvent-free formulation of paclitaxel that was initially developed more than a decade ago to overcome toxicities associated with the solvents used in the formulation of standard paclitaxel and to potentially improve efficacy. Nab-paclitaxel has demonstrated an advantage over solvent-based paclitaxel by being able to deliver a higher dose of paclitaxel to tumors and decrease the incidence of serious toxicities, including severe allergic reactions. To date, Food and Drug Administration (FDA) has indicated nab-paclitaxel for the treatment of three solid tumors. It was first approved for the treatment of metastatic breast cancer in 2005, followed by locally advanced or metastatic non-small-cell lung cancer in 2012, and most recently for metastatic pancreatic cancer in 2013. Nab-paclitaxel is also under investigation for the treatment of a number of other solid tumors. This study will be carried out as an audit for nab-paclitaxel in terms of clinical efficacy, safety outcomes as well as clinical perspective on the use of nab-paclitaxel in practice in the medical oncology department of Dubai Hospital (DH) over the last 3 years.

**Aim:** This study is aiming to identify the clinical perspective on the use of nab-paclitaxel in practice in the medical oncology department on Dubai Hospital (DH) to implement the accurate choice of nab-paclitaxel for our patients with prediction of best efficacy and safety profile for further usage.

**Patients and methods:** This retrospective descriptive study will include all the patients who received nab-paclitaxel in the medical oncology department of Dubai Hospital (DH) over the last 3 years (only 20 patients) treated from Jan.2015 until 12/2017. The data needs to be collected includes medical history, clinical, laboratory, radiological and pathological data, the treatment received and follow-up results of news scans, from patient records. Data will be recorded without identifiable information, so the researchers asked for waiving of informed consent because it is a retrospective study.

**Keywords:** Nab-paclitaxel; Objective response rate; Side effects

Abbreviations: SB: Solvent-Based; Nab-Paclitaxel: Albumin-Bound Paclitaxel; FDA: Food and Drug Administration; DHA: Dubai Health Authority; DH: Dubai Hospital; MTD: Maximum Tolerated Dose; AUC: Concentration-Time Curve; PFS: Progression-Free Survival; OS: Overall Survival; ORR: Objective Response Rate; ECOG: Eastern Cooperative Oncology Group; RECIST: Response Evaluation Criteria in Solid Tumors; NSCLC: Non Small Cell Lung Cancer

Introduction

Paclitaxel is widely used for the treatment of solid tumors [1-3]; however, the solvent used in the commercial formulation of solvent-based (sb)-paclitaxel, polyoxyethylated castor oil (Kolliphor® EL, formerly known as Cremophor EL; BASF SE, Ludwigshafen, Germany), is associated with severe, sometimes fatal hypersensitivity reactions [4-6]. To reduce the risk of hypersensitivity reactions with sb-paclitaxel, patients are routinely pretreated with corticosteroids and antihistamines.1,2 Furthermore, some studies have shown that Kolliphor EL can entrap paclitaxel in solvent micelles, making the drug less available to enter tumors, thereby limiting its clinical efficacy [6-8].

Nab-paclitaxel is a solvent-free albumin-bound form of paclitaxel [2,3,9]. Compared with sb-paclitaxel, nab-paclitaxel has several advantages, including the ability to deliver significantly higher doses of paclitaxel over a shorter infusion time (30 minutes vs 3 hours for sb-paclitaxel) and the elimination of the need for pre-medications to prevent hypersensitivity reactions. Other advantages of nab-paclitaxel over sb-paclitaxel include enhanced transport of paclitaxel across endothelial cells and greater delivery of paclitaxel to tumors. Because nab-paclitaxel is formulated with albumin, it is postulated that the drug uses endogenous albumin transport pathways, including receptor-mediated transcytosis, to cross endothelial cell monolayers and enter tumors [9,10]. In a
preclinical study, fourfold more nab-paclitaxel was transported across endothelial cells than sb-paclitaxel [9]. Moreover, it was found that Kolliphor EL inhibited the binding of paclitaxel to albumin and endothelial cells, potentially limiting intra-tumoral uptake of paclitaxel [9]. Albumin, or albumin-bound molecules such as nab-paclitaxel, may also find a way into the tumor microenvironment via the enhanced permeation and retention effect, which proposes that molecules are able to escape the circulation through gaps between endothelial cells resulting from leaky vasculature around tumors [11]. A comprehensive review of nab-paclitaxel’s mechanism of action and delivery system has recently been published [12].

Recent studies on the population pharmacokinetics (PK) and pharmacodynamics (PD) of nab-paclitaxel demonstrated that pharmacologic features of nab-paclitaxel appear to be distinct from those of sb-paclitaxel [13,14]. These distinct features likely contribute to the differences in clinical safety and efficacy between the two paclitaxel formulations [13]. Specifically, compared with sb-paclitaxel, nab-paclitaxel was associated with faster and deeper tissue penetration and slower elimination of paclitaxel. Tissue distribution of paclitaxel was found to be dependent on the drug carrier complex [14]. These results confirm preclinical findings that more paclitaxel may be able to enter the tumor when delivered as nab-paclitaxel [9] - and with more rapid distribution to tissues, the duration of high systemic exposure is shorter. This may, in turn, explain the observation of the lower frequency of some severe adverse events, such as neutropenia, with nab-paclitaxel than with sb-paclitaxel, despite that nab-paclitaxel demonstrates a higher paclitaxel dose intensity (26%–49% higher) than sb-paclitaxel [15-17].

Furthermore, in the population PK/PD study, a threshold plasma concentration for nab-paclitaxel was defined at 0.84 mM, such that the duration of time spent above this concentration predicted the probability of neutropenia [13]. Compared with that previously reported for sb-paclitaxel (0.05 mM), the threshold plasma paclitaxel concentration was nearly 17-fold higher for nab-paclitaxel [13]. Consistent with these findings, in trials to establish the maximum tolerated dose (MTD) of nab-paclitaxel, it was found that the albumin-bound formulation of paclitaxel allowed for a higher dose delivery of paclitaxel compared with sb-paclitaxel. The MTD of nab-paclitaxel was 71% to 88% higher than that reported for sb-paclitaxel for both the every-3-weeks (q3w) regimen (300 vs 175 mg/m²) and the weekly regimen (150 vs 80 mg/m²) in patients with advanced or metastatic solid tumors [18-20]. Dose-limiting toxicities in these trials included neutropenia, peripheral neuropathy, stomatitis, and superficial keratopathy [19-20]. With respect to peripheral neuropathy, a common taxane-associated side effect, the incidence of peripheral neuropathy with nab-paclitaxel compared to with sb-paclitaxel has varied across trials [15,16]. Differences in patient populations, dosing schedules, and adverse-event management strategies may have played a role in the varying incidence rates. Nevertheless, the ability to deliver a higher dose of paclitaxel and the enhanced tissue distribution and tumor uptake of nab-paclitaxel versus sb-paclitaxel likely contributes to the more favorable efficacy and safety profile of the albumin-bound formulation of paclitaxel.

### Breast Cancer

A Phase I dose-escalation trial of 19 patients with advanced solid tumors established the MTD of nab-paclitaxel at 300 mg/m² given q3w.18 Dose-limiting toxicities included peripheral neuropathy, stomatitis, and superficial keratopathy, which occurred at a dose of 375 mg/m². There were no reported hypersensitivity reactions despite the absence of steroid premedication and a short infusion time (30 minutes). The MTD and schedule were subsequently evaluated in a Phase II trial for the first- or second-line treatment of patients with metastatic breast cancer (MBC). The trial reported an overall response rate (ORR) of 48% for the intent-to-treat population of patients, with a 64% ORR in chemotherapy-naïve patients [21]. Time to tumor progression was 6.1 months and median overall survival (OS) was 14.6 months. These results supported the study of nab-paclitaxel vs sb-paclitaxel in a Phase III trial of patients with MBC [15]. In this study, the dose of nab-paclitaxel was reduced to 260 mg/m² q3w to lower the risk for severe toxicities, but the dose intensity was still 49% higher than that of sb-paclitaxel, which was dosed at 175 mg/m² q3w.15 Nab-paclitaxel demonstrated a significantly higher ORR (33% vs 19%; P=0.001; primary endpoint) and significantly longer time to tumor progression (5.3 vs 3.9 months; P=0.006) compared with sb-paclitaxel (Table 1). OS was not significantly different between the two paclitaxel treatments for the overall population (14.9 vs 12.8 months; P=0.374), but patients who received nab-paclitaxel as second-line or greater did have a significantly longer OS than those who received sb-paclitaxel (13.0 vs 10.7 months; hazard ratio [HR] 0.73; P=0.024). Grade 4 neutropenia was more common with sb-paclitaxel than with nab-paclitaxel (22% vs 9%), but the incidence of grade 3 sensory neuropathy was higher with nab-paclitaxel than with sb-paclitaxel (10% vs 2%) (Table 1). Sensory neuropathy was managed with dose interruptions or reductions and improved to grade 2 or less in a median of 22 days. Based on these positive results, nab-paclitaxel received its first US Food and Drug Administration (FDA) approval in 2005 for the treatment of MBC. Nab-paclitaxel is indicated for patients with breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy [3]. Prior therapy should have included an anthracycline unless clinically contraindicated.

### NSCLC

Another Phase II dose-finding study found that 100 mg/m² weekly nab-paclitaxel combined with q3w carboplatin area under the concentration-time curve (AUC) 6 provided the best clinical benefit-risk ratio compared with several other doses/schedules of nab-paclitaxel plus carboplatin but this time in patients with advanced NSCLC [22]. This dose/schedule showed comparable efficacy to the other dosing cohorts and had the least severe adverse events. These results led to a larger Phase III trial of more than 1,000 patients with advanced NSCLC in which the mentioned dose/schedule of nab-paclitaxel plus carboplatin was compared with 200 mg/m² sb-paclitaxel plus carboplatin AUC 6 q3w.16 This study met its primary endpoint with improvement in ORR for nab-paclitaxel plus carboplatin versus sb-paclitaxel plus carboplatin (33% vs 25%; P=0.005; Table 1). However, there was...
A subset analysis of the Phase III trial based on predefined stratification factors revealed that patients with squamous histology treated with nab-paclitaxel plus carboplatin had a significantly higher ORR compared with those who received sb-paclitaxel plus carboplatin (41% vs 24%; \(P<0.001\)). In addition, the median OS was significantly longer in patients 70 years of age who were treated with nab-paclitaxel plus carboplatin compared with sb-paclitaxel plus carboplatin (19.9 vs 10.4 months; \(P=0.009\)). In the overall treated population, grade 3 neutropenia (47% vs 58%) and sensory neuropathy (3% vs 12%) occurred significantly less frequently with nab-paclitaxel plus carboplatin (\(P=0.001\); Table 1), while grade 3 thrombocytopenia (18% vs 9%) and anemia (27% vs 7%) were more common with nab-paclitaxel plus carboplatin than with sb-paclitaxel plus carboplatin (\(P=0.001\)). The safety profiles were similar, regardless of patient age or histology [23,24]. Based on the findings of this Phase III trial, the FDA-approved nab-paclitaxel in combination with carboplatin for the first-line treatment of patients with locally advanced or metastatic NSCLC who are not candidates for curative surgery or radiation [3].

Table 1: Phase III Registration trials of albumin-bound paclitaxel (nab-p) in breast, non-small-cell lung, and pancreatic cancers.

<table>
<thead>
<tr>
<th>Phase III Trail</th>
<th>Patient Population</th>
<th>Regimen</th>
<th>Efficiency</th>
<th>Select Grade ≥AEs, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast Cancer</strong></td>
<td></td>
<td></td>
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<tr>
<td>Gradishar et al. [15]</td>
<td>First-line (n=97)</td>
<td>Nab-P 260 mg/m³ 30-minutes infusion q3w</td>
<td>ORR, % 33</td>
<td>Median PFS, mo 5.3</td>
</tr>
<tr>
<td></td>
<td>Second line or later (n=132)</td>
<td>sb-P 175 mg/m³ 3 hours infusion q3w</td>
<td>19 P=0.001</td>
<td>TTP 3.9</td>
</tr>
<tr>
<td><strong>Non small cell lung cancer</strong></td>
<td>Socinski et al. [16]</td>
<td>First line (n=521)</td>
<td>Nab-p 100mg/m² 3-hours infusion on day 1,8 and 15 followed by carbo AUC 6mg/mL/min on day 1 q3w</td>
<td>33 P=0.005</td>
</tr>
<tr>
<td></td>
<td>First line (n=531)</td>
<td>sb-P 200 mg/m³ 3 hours infusion + carbo AUC 6mg/mL/min, both given q3w</td>
<td>25</td>
<td>P=0.0214</td>
</tr>
<tr>
<td><strong>Pancreatic Cancer</strong></td>
<td>Von Hoff et al. [33]</td>
<td>First line (n=431)</td>
<td>Nab-p 125mg/m² 30 to 40-minutes followed by gem 1,000 mg/m³ on days 1,8 and 15 every 4 weeks</td>
<td>23 P&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>First line (n=430)</td>
<td>Gem 1,000 mg/m³ weekly for 7 of 8 weeks (cycle 1) and then on days 1,8 and 15 every 4 weeks</td>
<td>7 P&lt;0.001</td>
<td>3.7</td>
</tr>
</tbody>
</table>

Note: *Grade 3 only
AEs: Adverse Events; AUC: Area Under The Concentration-Time Curve; Carbo: Carboplatin; Gem: Gemcitabine; Nmo: Month; ORR: Overall Response Rate; OS: Overall Survival; PFS: Progression Free Survival; Q3w: Every 3 Weeks, Sb-P: Sb-Paclitaxel; TTP: Time to Progression

Pancreatic Cancer
Nab-paclitaxel also got FDA approval in pancreatic cancer. For long time Gemcitabine monotherapy is one of the most widely used agents in the treatment of metastatic pancreatic cancer, based on a seminal study by Burris et al that demonstrated a median survival of ≈6 months [25]. A decade later and after numerous failed clinical trials, erlotinib in combination with gemcitabine was FDA approved for the treatment of locally advanced, unresectable, or metastatic pancreatic cancer [26], partly based on a statistically significant 0.3-month survival advantage for erlotinib plus gemcitabine vs gemcitabine alone [27]. However, in routine clinical practice, this combination is very selectively used in a small subset of patients. Several other Phase III trials of gemcitabine doublets failed to demonstrate a significant survival advantage over gemcitabine alone [25,27-32]. Nab-paclitaxel was selected as a combination partner for gemcitabine because it has been shown to synergize with gemcitabine and was associated with increased intra-tumoral...
delivery of gemcitabine and stromal depletion.33 In a Phase I/II trial, the MTD of nab-paclitaxel in combination with 1,000 mg/m² gemcitabine was established at 125 mg/m²; both agents were given weekly for the first 3 of 4 weeks (qw 3/4) in patients with advanced pancreatic cancer [33,34]. For patients treated at the MTD (n=44), the ORR was 48% and median OS was 12.2 months. This led to a large multinational Phase III trial of more than 850 patients in who 125 mg/m² nab-paclitaxel plus 1,000 mg/m² gemcitabine qw 3/4 was compared with 1,000 mg/m² gemcitabine alone (given weekly for 7 of 8 weeks during cycle 1 and then qw 3/4 for cycle 2 and beyond) [Table 1] [35]. Median OS (primary endpoint) was significantly longer with nab-paclitaxel plus gemcitabine versus gemcitabine alone (8.5 vs 6.7 months; P<0.001). The treatment benefit of nab-paclitaxel plus gemcitabine over gemcitabine alone was consistent across most pre-specified subgroups, including those patients with more advanced disease (eg, poorer performance status, liver metastasis, 3 sites of metastatic disease, and carbohydrate antigen 19-9 levels > 59× the upper limit of normal) [35]. Grade 3 neutropenia (38% vs 27%), fatigue (17% vs 7%), and neuropathy (17% vs 1%) were higher with nab-paclitaxel plus gemcitabine versus gemcitabine alone; no patients experienced grade 4 neuropathy in either arm. As observed in other trials [15,16,36] the grade 3 neuropathy associated with nab-paclitaxel resolved for a majority of patients and improved to grade 1 or lower in a median of 29 days.

Nab-paclitaxel plus gemcitabine was the first gemtuzumab ozogamicin doublet to demonstrate a clinically meaningful benefit over gemcitabine alone in a Phase III trial of advanced/metastatic pancreatic cancer [25,27-32]. In 2013, nab-paclitaxel plus gemcitabine became an FDA-approved regimen for the first-line treatment of patients with metastatic pancreatic cancer [3].

Based on the hypothesis of secreted protein acidic and rich in cysteine (SPARC), an albumin-binding protein, playing a role in the delivery of nab-paclitaxel to tumors, analyses have been performed to examine the relationship between SPARC expression and outcome in patients treated with nab-paclitaxel plus gemcitabine. In the Phase I/II trial, high versus low stromal SPARC expression was associated with longer OS in the nab-paclitaxel plus gemcitabine arm (17.8 vs 8.1 months; P=0.0431), suggesting that SPARC may be a biomarker for pancreatic cancer that facilitates accumulation of nab-paclitaxel into tumors [33]. An analysis of SPARC status in the Phase III Metastatic Pancreatic Adenocarcinoma Clinical Trial found that stromal, tumor, and plasma SPARC were not prognostic for survival or predictive of survival in either treatment arm [37].

**Patients and Methods**

**Study location**

The study will be conducted at the medical oncology department of Dubai Hospital, Dubai Health authority, Dubai.

**Inclusion criteria**

All the patients who have been treated with nab-paclitaxel in the medical oncology department of Dubai Hospital over the last 3 years (between January 2015 till December 2017).

**Exclusion criteria**

Patients who discontinued the treatment with nab-paclitaxel by their own without developing toxicity or Side effects.

**Study design**

the study will be a retrospective descriptive study which will collect all the required data from the filing records in Dubai hospital for the selected group of patients using either the old paper files and the new electronic medical record system, which through both of them we can access the clinical, laboratory, radiological and pathological data in addition to treatment regimens, tolerability and response evaluation.

**Aim**

This study is aiming to identify the clinical perspective on the use of nab-paclitaxel in practice in the medical oncology department on Dubai Hospital (DH) to implement the accurate choice of nab-paclitaxel for our patients with prediction of best efficacy and safety profile for further usage.

**Objectives**

**Primary objectives**

A. To assess the objective response rate (ORR) of nab-paclitaxel in our patients in comparison to the literature.

B. To shortlist the possible toxicities and side effects of nab-paclitaxel and magnitude of its toxicity for our patients.

**Secondary objectives:** Understand the pattern of use of nab-paclitaxel in practice in the medical oncology department on Dubai Hospital over the last 3 years.

**Structural format of data from medical records includes**

**Personal history:** This includes age at the start of nab-paclitaxel regimens, gender, diagnosis and stage of cancer, Eastern Cooperative Oncology Group (ECOG) performance status:

- 0 - Asymptomatic (Fully active, able to carry on all predisease activities without restriction)

- 1 - Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work)

- 2 - Symptomatic, <50% in bed during the day (Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours)

- 3 - Symptomatic, >50% in bed, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours)

- 4 - Bed bound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair)

- 5 - Death

**Investigations:** Baseline radiological assessment and then during
follow up and after receiving of nab-paclitaxel (x-ray, ultrasound, computerized tomography-CT, magnetic resonance imaging- MRI or PET CT scan). The response to chemotherapy will be assessed according to Response Evaluation Criteria in Solid Tumors (RECIST) from the patients’ medical records of pre and post chemotherapy imaging (x-ray, ultrasound, CTs, MRI or even PET CT scans) as follows:

A. Complete Response (CR): Disappearance of all target lesions.
B. Partial Response (PR): At least a 30% decrease in the sum of the longitudinal diameter LD of target lesions, taking as reference the baseline sum LD.
C. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started.
D. Progressive Disease (PD): At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions.

**Statistical analysis**

A. Data will be analyzed by using the Statistical Package of Social Science (SPSS). Version 15 (SPSS Inc., Chicago, L, USA)
B. Data entry and analysis by using the “SPSS 15.0” by aid of the following statistical tests:
C. Continuous variables are presented as means ± standard deviation (SD).
D. Discrete variables are expressed as frequencies and percentages.
E. Chi square and the Fishers exact test will be used to test significance of the difference between qualitative data.
F. Probability value (P) <0.05 is considered statistically significant.
G. Presentation of the statistical outcomes and tables will be performed using the “Microsoft Word 2013” program.
H. The results will be expressed in tables and graphs.

**Results**

Between January 2015 and December 2017 Nab-paclitaxel was requested for around 30 patients in the medical oncology department of Dubai hospital but actually 22 patients only were able to start it while around 8 patients could not start due to financial problems. Out of those 22 patients, 20 patients inclined their plan of treatment, while 2 of them discontinued the treatment with nab-paclitaxel by their own without developing toxicity or Side effects.

Therefore, the retrospective audit on the use of Nab-paclitaxel in the medical oncology department, Dubai hospital as per the inclusion criteria, was done on the 20 patients who met the inclusion criteria.

The majority of patients (N= 17): 85% were females, while only male patients were 3 (15%), the minimum age of the included patients was 30 years old, the maximum was 80 years old & the average age was 54.8 years old.

The three male patients were diagnosed to have metastatic pancreatic cancer, while the remaining seventeen female patients had metastatic breast cancer and all patients were receiving dose of 100mg/m² D1,8&15 every 3 weeks.

There were no reported cases of hypersensitivity reactions with Nab-paclitaxel. However, 4 patients (20%) could not manage to complete the planned treatment with Nab-paclitaxel due to poor tolerance and Grade III/IV toxicities. Those included grade 4 neutropenia which was documented in 2 patients (10%) and had to discontinue the treatment, in addition to grade 3 sensory neuropathy was documented in 1 patient (5%) who could not tolerate and we had to discontinue his treatment, Plus 1 patient was reported because she developed severe resistant cellulitis of both lower limbs and we also had to discontinue her treatment.

The initial response assessment interval in months for all the included patients between the baseline scans and next scans ranged between 2-4 months with average of 2.8 months.

The restating scans which showed stable disease in 3 patients out of the total 20 representing (15%) and this was considered as desirable response and they were kept on the same Nab-paclitaxel regimen. Partial response was appreciated in 7 patients representing (35%) of the total number of patients while complete responses was achieved in only 1 patient (5%).

The Initial restating scans showed progression of the disease in 5 patients representing (25%) of the total number of patients while 4 patients (20%) could not manage to complete the planned treatment with Nab-paclitaxel due to poor tolerance and Grade III/IV toxicities and had to discontinue the treatment in the first month.

So the overall response rate was 55% and the average time to tumor progression was 6 months with range between 3 months up to 20 months.

**Discussion**

In this retrospective study we found that; in the medical oncology department in Dubai Hospital, the total number of patients who were treated with Nab-paclitaxel from January 2015 until December 2017 is (20 patients) although it was as well noted that Nab-paclitaxel was requested for around 30 patients but actually 22 patients only were able to start it while around 8 patients could not start due to financial problems and out of those 22 patients, 20 patients inclined their plan of treatment, while 2 of them discontinued the treatment with nab-paclitaxel by their own without developing toxicity or Side effects; which actually reflect other kind of toxicities which is financial toxicity that is in agreement with Shankaran V, Ramsey S. Addressing that the cost of comprehensive cancer therapy remains a significant Burden to the healthcare system [38,39].
Although Nab-paclitaxel got FDA approval in 3 disease areas in oncology including breast cancer, pancreatic cancer and non-small cell lung cancer with different indications \([3,23,24,37]\), it was only used in 2 disease areas only; metastatic pancreatic cancer or metastatic breast cancer but was not used in lung cancer over the same period of time and this reflect the presence of many alternative options for treatment of locally advanced or metastatic NSCLC who are not candidates for curative surgery or radiation \([3]\). The recommended dose and schedule for nab-paclitaxel in metastatic pancreatic cancer is 125 mg/m\(^2\) on days 1, 8, and 15 of each 28-day cycle, while the recommended dose of nab-paclitaxel in metastatic breast cancer is 260 mg/m\(^2\) administered intravenously over 30 minutes every 3 weeks \([3,25,27-32]\), however it was noticed that Nab-paclitaxel was given for all patients either metastatic breast cancer or metastatic pancreatic cancer in dose of 100mg/m\(^2\) D1,8&15 every 3 weeks which was found to be more convenient for physicians and may be with less toxicity profile.

Data from the Phase III trial / FDA approval study of nab-paclitaxel in metastatic breast cancer which compared sb-paclitaxel with nab-paclitaxel showed that grade 4 neutropenia was more common with sb-paclitaxel than with nab-paclitaxel (22% vs 9%), but the incidence of grade 3 sensory neuropathy was higher with nab-paclitaxel than with sb-paclitaxel (10% vs 2%). While in the Phase III trial / FDA approval study of nab-paclitaxel in metastatic pancreatic cancer which compared nab-paclitaxel plus gemcitabine versus gemcitabine alone it was reported that; Grade 3 neutropenia (38% vs 27%), and neuropathy (17% vs 1%) was higher with nab-paclitaxel plus gemcitabine versus gemcitabine alone; no patients experienced grade 4 neuropathy in either arm.15,16,36. In this study 3 patients only were diagnosed to have metastatic pancreatic cancer and 17 patients had metastatic Breast cancer; so because of low number of patients further classification of patients to subgroups may affect the statistics, however overall grade III/IV toxicities was documented in 4 patients (20%). Half of them (10% of the total number of patients) developed grade 4 neutropenia and advised to discontinue the treatment, 1 patient (5%) developed grade 3 peripheral neuropathy and could not tolerate to continue the treatment as well, in addition to 1 patient who was reported that she developed severe resistant cellulitis of both lower limbs and we had to discontinue her treatment but for this particular patient we could not fully assess the relation between use of Nab-paclitaxel and this severe resistant cellulitis because by reviewing this case it was noticed that this patient had diabetes mellitus and her HBA1c during the same period of receiving the Nab-paclitaxel was 9.6%.

The FDA approval Phase II study of ab-paclitaxel in metastatic breast cancer which compared sb-paclitaxel with nab-paclitaxel revealed that Nab-paclitaxel demonstrated a significantly higher ORR (33% vs 19%; P=0.001) and significantly longer time to tumor progression (5.3 vs 3.9 months; P=0.006) compared with sb-paclitaxel \([3,15]\). However, in this study, the overall response rate was 55% and the average time to tumor progression was 6 months with range between 3 months up to 20 months.

The overall response rate was as follows 3 patients out of the total 20 representing (15%) had stable disease and this was considered as desirable response and they were kept on the same Nab-paclitaxel regimen. Partial response was appreciated in 7 patients representing (35%) of the total number of patients while complete responses was achieved in only 1 patient (5%).

Conclusion

A. Nab-paclitaxel is currently the only FDA- and European Medicines Agency-approved encapsulated form of paclitaxel \([3,40]\).

B. Nab-paclitaxel represent is an important option in the treatment of metastatic breast cancer and the best option in metastatic pancreatic cancer in combination with Gemcitabine, however in advanced or metastatic NSCLC in not a priority option for most of physician due presence of lots of alternative options.

C. The cost of comprehensive cancer therapy remains a significant Burden to the healthcare system \([38,39]\).

D. Number of Phase II trials in other solid tumors, including urothelial, squamous-cell carcinoma of the head and neck \([41]\), gastric cancer \([42]\), and colorectal and small bowel carcinoma \([43]\), are ongoing and should provide us with information regarding the role of nab-paclitaxel in the treatment of these tumor types as well. In addition to other studies in breast cancer, NSCLC, and pancreatic cancer are currently under investigation and may lead to expanded indications of nab-paclitaxel in these disease areas \([44-44]\).

E. Differences in efficacy and safety between these paclitaxel formulations remain to be determined in more future clinical trials.

Acknowledgement

None.

Conflict of Interest

Authors declare there is no conflict of interest in publishing the article.

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