Research Article

The Clinical Lung Cancer

A randomized placebo-controlled clinical study of nab-paclitaxel as second-line chemotherapy for patients with advanced non-small cell lung cancer in China.

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INTRODUCTION

In China and around the world, lung cancer is the most common type of cancer to be diagnosed and the primary cause of cancer-related fatalities [1]. In 2012, there were an estimated 1.8 million new instances of lung cancer, making up roughly 13% of all cancer diagnoses [2]. Over 80% of cases of lung cancer are not minor ones.NSCLC (small cell lung cancer) [3]. While patients with localized NSCLC have a 5-year survival rate of over 50%, 57% of patients had progressed or metastatic NSCLC at diagnosis, which has a 5-year survival rate of only 5% [4]. A platinum-based doublet comprising third-generation cytotoxic drugs (such as carboplatin plus paclitaxel or cisplatin plus gemcitabine) is the recommended first-line treatment for advanced non-small cell lung cancer (NSCLC) in the absence of targetable genetic abnormalities [5,6]. Numerous individual chemotherapy regimens, such as those including gefitinib, erlotinib, pemetrexed, and docetaxel, have therapy of advanced non-small cell lung cancer (2012) [9, 10]. In patients with advanced non-small cell lung cancer (NSCLC), a phase III trial showed that nab-paclitaxel plus carboplatin considerably increased overall response rates when compared to traditional, solvent-based paclitaxel plus carboplatin [11]. More and more data have suggested that nab-paclitaxel, either alone or in conjunction with gemcitabine as a chemotherapeutic reagent, can be employed as the second-line treatment for gastric cancer [14] or pancreatic cancer [12, 13] that increases patient survival rates. Nevertheless, there is currently insufficient data to determine if nab-paclitaxel is a useful second-line chemotherapy treatment for patients with advanced non-small cell lung cancer. Consequently, we assessed the safety and effectiveness of nab-paclitaxel as a single reagent as a second-line therapy for patients who have progressed in this phase II clinical trial, which is randomized and placebo-controlled, in China.

MATERIALS AND PROCEDURES

Declaration of ethics

The current study's protocols were all carried out in compliance with the Declaration of Helsinki and Good Clinical Guidelines for Practice. The People's Hospital in Dongyang City's ethics committees examined and authorized every procedure and treatment. Each patient who took part signed the consent forms.

Patients

Participants in the current study were 92 eligible patients with advanced non-small cell lung cancer (NSCLC) who were seen at the People's Hospital of Dongyang city in Dongyang, Zhejiang province, China, between October 2011 and October 2014. Individuals suffering from Two treatment groups, one with nab-paclitaxel (46 patients) and the other with placebo-controlled (46 patients), were randomly stratified (in a 1:1 ratio) for advanced NSCLC. Participants in the study had to meet certain criteria in order to be considered: they had to be between the ages of 18 and 75, have an advanced non-small cell lung cancer (NSCLC) with a performance status (PS) between 0 and 3, have received first-line platinum-based chemotherapy but the disease was still progressing, have a minimum life expectancy of three months, and have adequate hepatic, renal, or bone marrow functions.

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Design and management of the study

The effectiveness and safety of nab-paclitaxel as second-line chemotherapy for Chinese patients with advanced non-small cell lung cancer (NSCLC) following platinum-based chemotherapy are being assessed in this open-label, placebo-controlled, randomized phase II clinical research. failure of first-line chemotherapy.

Two weeks before to the study, chest and abdominal computed tomography scans were taken. For patients to be assessed for a response, they had to have at least one detectable lesion.

In order to administer medication, patients in the nab-paclitaxel group received 150 mg/m2 intravenously on days 1, 8, and 15 of a 4-week cycle. Patients should be treated for at least two cycles, with a maximum of six cycles, until they are unable to handle the adverse events (AEs) or request to stop the treatment.

Analytical statistics

Response rates (RRs) served as the study's main objective. Overall survival (OS), progression-free survival (PFS), or adverse events (AEs) were the secondary goals. To estimate OS and PFS, the Kaplan–Meier approach was used.The comparison PFS and OS measurements were made using a log-rank test with a 95% confidence interval (CI).

RESULTS

Individuals

A total of 92 individuals with advanced NSCLC were eligible for the study between October 2011 and October 2014. In a 1:1 ratio, they were assigned at random to the nab-paclitaxel group (n=46) and the placebo-controlled group (n=46). The percentages of male and female patients in the placebo-controlled group and the nab-paclitaxel group were 56.5%/43.5% and 52.2%/47.8%, respectively, as Table 1 illustrates.The average ages were 58.5 years (23–74 years) in the nab paclitaxel group and 57.2 years (25–73 years) in the placebo-controlled group, respectively.More than 90% of patients in both groups had ECOGPS between 0 and 2, more than 90% of patients were current or former smokers, and almost 70% of patients had adenocarcinoma. Following first-line platinum-based chemotherapy, 32.6 and 30.4% of patients in the placebo-controlled group and the nab-paclitaxel group, respectively, showed responses. Additionally, 50.0 and 54.3% of patients in the placebo-controlled group and the nab-paclitaxel group, respectively, had constant disease percentages.The clinical characteristics and baseline demographics did not significantly differ, indicating that the baseline characteristics of the patients were evenly distributed across the two groups.

Efficacy

The current study's cutoff date was October 4, 2014, and the course of treatment lasted roughly two to six months.Table 2 summarises the RRs for patients in the placebocontrolled group and the ab-paclitaxel group.The estimated total RRs for the two groups were 2.2%(1/46) in the nab-paclitaxel group and 0.0%(0/46) in the placebo-controlled group.Positively, the partial RR in the b-paclitaxel group was significantly higher (17.4%, 8/46) than in the placebo-controlled group (4.3%, 2/46) (P<0.001).With a considerable improvement, the objective RR went from 4.3 (2/46) in the placebo-controlled group to 19.6% (9/46) in the nib-paclitaxel group (P<0.001).Additionally, the stable disease dramatically improved as well, going from 15.2(7/46) in the placebo-controlled group to 52.2%(24/46) in the group receiving naproxene (P<0.001).The verified progressive disease rates were 43.5% (20/46) in the non-b-paclitaxel group and 67.4 (31/46) in the placebo-controlled group. The two groups' median PFS and OS were compared (Figure 1).The PFS for nab paclitaxel was 4.6 months (95%CI: 3.4–6.7 months), while the PFS for placebo was 2.0 months (95%CI: 0.9 4.3 months), indicating a 56% decline in the course of the illness (hazard ratio:0.62; 95% confidence interval: 0.33-0.81; P<0.001). The median overall survival (OS) for nab-paclitaxel was 6.3 months (95%CI:3.9-8.2 months), while the placebo had a median OS of 4.9 months (95%CI:2.1-5.9 months). This indicates a 22% decrease in the course of the disease (hazard ratio:0.71; 95% CI: 0.33–0.85; P<0.001).

Safety

The two groups' Grades 3 and 4 AEs were compared (Table 3). The overall rates of grades 3 and 4 adverse events (AEs) were 34.8% (16/46) for nab-paclitaxel and 6.5 (4/46) for placebo-controlled groups. Diarrhoea was the most common grade 3 or 4 adverse event in both groups, affecting 4.3 (2/46) of all patients in the placebo-controlled group and 13.0% (6/46) of all patients in the nab-paclitaxel group.Other grades 3 and 4 AEs in the placebo-controlled group were fatigue (2.2%, 1/46), thrombocytopenia (2.2%, 1/46), leucopenia (4.3%, 2/46), and nausea (2.2%, 1/46). Other grades 3 and 4 AEs in the enab-paclitaxel group included fatigue (13.0%, 6/46), infection (10.9%, 5/46), leucopenia (10.9%, 5/46) and rash (8.7%, 4/46).

DISCUSSIONS

The current study examined the safety and effectiveness of nab-paclitaxel used alone as a second-line chemotherapy treatment for Chinese patients with advanced non-small cell lung cancer (NSCLC). It was conducted as a randomised, placebo-controlled phase II trial. According to our research, the objective response improved dramatically with nab-paclitaxel, going from 4.3 (2/46) for placebo to 19.6% (9/46) for the drug. Additionally, we demonstrated that nab-paclitaxel

dramatically improved PFS and OS.PFS increased in the nab-paclitaxel group from 2.0 (95% CI: 0.9–4.3 months) to 4.6 months (95% CI: 3.4–6.7 months) (hazard ratio:0.62; 95% CI: 0.33–0.81; P<0.001). The group receiving nab-paclitaxel had a better median overall survival (OS) with a difference of 6.3 months (95% CI: 3.9–8.2 months) compared to 4.9 months (95% CI: 2.1–5.9 months) in the placebo-controlled group (hazard ratio:0.71; 95% CI: 0.33–0.85; P<0.001).

At now, the FDA has approved docetaxel, permetrexed, and lerlotinib as second-line chemotherapeutic medicines for patients suffering from non-small cell lung cancer. Shepherd-style. [15]ran a phase III, randomised, placebo-controlled, double-blind experiment to find out if erlotinib extended survival in non-small cell lung cancer (NSCLC) patients when first- or second-line chemotherapy failed. Erlotinib (150 mg q.d.) was found to significantly improve PFS (2.2 months against 1.8 months for placebo, P<0.001) and OS (6.7 months versus 4.7 months for placebo, P<0.001) in patients with stage IIIB or IV NSCLC who did not respond to first- or second-line therapy.Hannaet al. [16] evaluated the safety and effectiveness of pemetrexed against docetaxel in patients with advanced non-small cell lung cancer who had received prior chemotherapy during a phase III trial.It was shown that the median PFS (2.9 months compared with 2.9 months, P>0.05) and median survival time (8.3 months compared with 7.9 months, P>0.05) were similarly effective for pemetrexed and docetaxel.Lietal.[17] looked into the impact of ferrlotiniband pemetrexedone themedian PFS in patients with EGFR wild type lung cancer who had previously received chemotherapy with one platinum atom.Themelian PFS was found to be 4.1 months (95%CI:1.6-6.6 months) in the erlotinib group and 3.9 months (95%CI:2.7-5.1 months) in the pemetrexed group.Huand Zhang [18] found that the themesian PFS of patients with advanced non-small cell lung cancer (95%CI: 1.9–5.8 months) following first-line platinum-based chemotherapy was 3.5 months when ab-paclitaxel 100mg/m(2) (i.v.) was administered on days 1, 8, and 15 of a 28-day cycle.Liuetal.[19]PFS of patients with advanced non-small cell lung cancer (NSCLC) was compared after ineffective first-line chemotherapy, and the findings indicated that b-paclitaxel had a better PFS (5.1 months) than pemetrexed (4.6 months).Similarly, our research demonstrated the good efficacy of ab-paclitaxel in PFS (4.6 months).However, this result was the result of multiple circumstances in the current investigation.Initially, the current study's sample size was less than that of the earlier trials.A sizable patient pool with multi-center research would produce survival rates that are more accurate. Second, the present study exclusively included Chinese patients, and the variations in survival between these studies most likely stemmed from these ethnicity differences.Third, there were inevitable and unanticipated errors in this multicenter trial. The patients in the nab-paclitaxel group were shown to have a higher likelihood of experiencing grade 3 or 4 adverse events (AEs) compared to the placebo-controlled group.Abetaclitaxel had a total incidence rate of 34.8% for grade 3 or 4 AEs. The shepherdetal [15] revealed that 19% of the erlotinib group needed dose reductions due to drug-related toxic effects, and 26 patients (5%), stopped treatment as a result of these severe toxic effects.Rash(12%) and diarrhea(5%) were the most common adverse events among them.Hanna et al. [16] demonstrated that patients receiving docetaxel had higher rates of grade 3 or 4 neutropenia (40.2% versus 5.3%, P<.001), neutropenia with infections (13.4% versus 1.5%, P<.001), hospitalisations for neutropenic fever (10.15% versus 6.4%, P=0.092), and hospitalisations for other drug-related adverse events (11.5% versus 6.4%, P<.001) when compared to patients receiving metronidase.According to Cappuzzo et al. [20], rash (9%), and diarrhoea (2%), were the most frequent grade 3 adverse events (AEs) of erlotinib therapy.According to Liuetal [19], in patients with advanced non-small cell lung cancer undergoing pemetrexed treatment, the most common grade 3/4 adverse events (AEs) were rash (n = 4,7.1%), nausea (n = 2,3.6%), paronychia (n = 2,3.6%), anorexia (n = 2,3.6%), and thrombocytopaenia (n = 2,3.6%).As a result, the toxicity rates in this research were comparable to those of erlotinib and docetaxel, but they appeared to be marginally higher than those of pemetrexed.

Overall, our study's encouraging findings suggested that nab-paclitaxel might be utilised as a novel chemotherapeutic drug for patients with advanced non-small cell lung cancer (NSCLC) receiving second-line treatment.

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Authorcontribution

WuYueming: drafting of the manuscript; Feng Jiang: patient recruitment, admission and management; Hu Weiwei: patient management, statistics; Luo Qingquan: assistance wiyh project design.

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