ORIGINAL ARTICLE

WILEY

PEG-rhG-CSF for prophylaxis of neutropenia after chemotherapy in patients with non–small cell lung cancer: A multicenter, prospective, randomized study

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Abstract

Background: To evaluate the efficacy and safety of pegylated recombinant human granulocyte colony-stimulating factor (PEG-rhG-CSF) in preventing neutropenia during multiple cycles of chemotherapy in patients with non–small cell lung cancer (NSCLC).

Method: In a multicenter, prospective, randomized trial, patients with NSCLC were randomly assigned in a 2:1 ratio to treatment group (PEG-rhG-CSF as primary prophylactic therapy) or control group. Patients in the control group were administered rhG-CSF when white blood cell count was $<2.0 \times 10^9$/L or absolute neutrophil count $<1.0 \times 10^9$/L. The primary endpoint was the incidence of grade 3/4 neutropenia. Secondary endpoints included the incidence and duration of grade 3/4 neutropenia in each cycle, the incidence of febrile neutropenia (FN), delay rate of chemotherapy, prolonged time of chemotherapy, and safety.

Results: Between January 2019 and July 2021, 130 patients were enrolled (treatment group: $n = 87$, control group: $n = 43$). The incidence of grade 3/4 neutropenia in the treatment group was significantly lower than that in the control group (1.15% vs. 11.63%, $p < 0.05$). The mean duration of grade 3/4 neutropenia for the treatment and control group was 2.00 and 3.75 days, respectively. There were no statistical differences in the incidence of FN, delay rate of chemotherapy, prolonged time of chemotherapy, and antibiotic use between the two groups (all $p > 0.05$). Adverse events were reported in 47.13% of patients in the treatment group and 48.84% patients in the control group.

Conclusions: Primary prophylactic treatment with PEG-rhG-CSF could reduce the incidence of neutropenia in patients with NSCLC during multiple cycles of chemotherapy, with acceptable safety and tolerability.

KEYWORDS
multiple cycles of chemotherapy, neutropenia, non–small cell lung cancer, PEG-rhG-CSF, primary prophylactic

INTRODUCTION

Lung cancer is one of the most common types of cancer and the leading cause of cancer-related deaths worldwide,[1–3] with more than 1.59 million deaths.[4] Among the two major types of lung cancer, non–small cell lung cancer (NSCLC) and small cell lung cancer, ~85% of lung cancer patients are diagnosed with NSCLC.[5] Because of diagnosis at advanced stages, the 5-year survival of NSCLC is only ~20%–30%.[6] Conventional chemotherapy is the standard treatment

option for patients with NSCLC. Unfortunately, chemotherapy-related toxicities can always adversely affect the patient's tolerance to chemotherapy and limit the effectiveness of chemotherapy in clinical practice. Neutropenia is the major dose-limiting toxicity of chemotherapy and is commonly found in patients with lung cancer who are treated with platinum-based chemotherapy. Moreover, neutropenia will increase the risk for infection presenting as febrile neutropenia (FN), which can lead to chemotherapy dose reductions and delays, hospitalizations, and death.[7,8] Therefore, the prophylaxis strategy against FN is an important clinical issue.

Recombinant human granulocyte colony-stimulating factor (rhG-CSF) in clinical practice has emerged as effective supportive therapy for reducing the incidence of neutropenia and FN in cancer patients receiving chemotherapy.[9–11] However, it has a short plasma half-life of about 3–4 hours, requiring daily subcutaneous injections.[12] Pegylated rhG-CSF (PEG-rhG-CSF) is a long-acting derivative of rhG-CSF with increased molecular weight (39 kDa). It increased stability, decreased opportunity for enzymatic hydrolysis, prolonged plasma half-life (30–60 hours),[13] and decreased fluctuations in blood drug concentrations.[12,14] It is only required to administer PEG-rhG-CSF once per chemotherapy cycle. Therefore, the clinical application is much more convenient, and the pain from repeated injections was reduced. Sakaguchi et al.[15] found that prophylactic use of PEG-G-CSF (especially for primary use) was associated with better outcomes for progression-free survival (PFS) and overall survival (OS) in patients with advanced NSCLC treated with ramucirumab plus docetaxel. A multicenter, randomized, phase III trial in patients with breast cancer showed that the use of PEG-rhG-CSF was associated with a significantly lower incidence of grade ≥3 neutropenia.[16] However, whether PEG-rhG-CSF can better support patients with NSCLC in multiple cycles of chemotherapy remain unclear. This study analyzed the efficacy and safety of PEG-rhG-CSF in the prevention of neutropenia caused by multiple cycles of chemotherapy in patients with NSCLC. The results may provide a basis for the clinical application of PEG-rhG-CSF in the treatment process of multiple cycles of chemotherapy in patients with NSCLC.

METHODS

Study design and patients

This was a multicenter, prospective, randomized, open-label trial conducted in China between January 2019 and July 2021. Eligible patients met the following criteria: an age ranging from 18 to 70 years old; histologically/cytologically confirmed NSCLC; required multiple cycles of adjuvant chemotherapy; planned to accept a platinum-containing two-drug program; Karnofsky performance scores (KPS) ≥70; expected survival ≥3 months; adequate hematopoietic, liver, heart, and kidney functions. Patients were excluded if they had uncontrolled infection with temperature ≥38°C, had a history of stem-cell

or organ transplantation, underwent pregnancy or breast-feeding, declined to receive appropriate contraception methods in women of reproductive age, had allergies to PEG-rhG-CSF or rhG-CSF or other genetically engineered *Escherichia coli*-derived biological agents, had severe mental or neurological disorders affecting informed consent, and/or adverse reaction presentations or observations.

The protocol was approved by the ethics committee of the Fourth Hospital of Hebei Medical University, and all patients provided written informed consent. This study was conducted in accordance with the Declaration of Helsinki,[17] Good Clinical Practice, and all applicable regulatory requirements. This study was registered in the Chinese Clinical Trial Registry, number ChiCTR1800020351.

Randomization and masking

Patients were randomly assigned in a 2:1 ratio to receive or not receive PEG-rhG-CSF (treatment group) or rhG-CSF (control group). Randomization was done by a computer-generated program. Study coordinators, clinicians, investigators who did the statistical analyses, and the patients themselves were aware of the assignment.

Procedure

Patients in the treatment group received PEG-rhG-CSF (CSPC Baike Biopharmaceutical) once subcutaneously 48 hours after chemotherapy (weight, ≥45 kg, 6 mg once; weight, <45 kg, 3 mg once). If patients experienced white blood cell count (WBC) $<2.0 \times 10^9$/L or absolute neutrophil count (ANC) $<1.0 \times 10^9$/L in the control group, daily rhG-CSF was given until WBC $\geq4.0 \times 10^9$/L or ANC $\geq2.0 \times 10^9$/L. Otherwise, rhG-CSF was not allowed during the chemotherapy period. The interruption or reduction of the drug dose was decided by physicians.

For patients who received a 21-day chemotherapy regimen, blood was collected on days 0, 7, 9, 11, and 21 of each cycle (day 0 is defined as the day before each cycle) for blood routine inspection. For the 28-day chemotherapy regimen, blood samples were collected on days 0, 7, 9, 11, and 28 of each cycle for routine blood tests. If there was no return to normal after chemotherapy, blood count should be checked every odd number of days until normal or after suffering 14 days.

Endpoints

The primary endpoint was the incidence of grade 3/4 neutropenia in each cycle of chemotherapy. Grade 3/4 neutropenia was defined as ANC $<1.0 \times 10^9$/L. The incidence of grade 3/4 neutropenia was calculated by the following equation: the incidence of grade 3/4 neutropenia = $N_a \times 100\%/N_b$ (N_a, the number of patients who experienced grade 3/4

neutropenia in each group; N_b, the number of total patients in each group). The secondary endpoints included the incidence and duration of grade 3/4 neutropenia in each cycle of chemotherapy, the incidence of FN, antibiotic use, delay rate of chemotherapy, prolonged time of chemotherapy, and the administration of rhG-CSF. FN was defined as an ANC $<0.5 \times 10^9$/L or an ANC $<1.0 \times 10^9$/L with a trend to drop below 0.5×10^9/L within the next 48 hours, accompanied by a single oral temperature of $\geq 38.5°$C, or a temperature $\geq 38°$C for a duration of over 1 hour (or axillary temperature $>38.5°$C for more than 1 hour). Adverse events (AEs) could be reported at any time during the study after patient consent and up to 30 days from the last dose of the study drug. AEs were graded according to the Common Terminology Criteria for AEs version 5.0.[18]

Statistical analysis

The sample size of the trial was calculated using PASS Software by considering a two-sided alpha-level of 0.05, an 80% power, assuming a dropout rate of 10%. According to our experience, the incidence of neutropenia in the treatment group and control group was 16% and 42%, respectively. Considering these parameters, a sample size of at least 120 patients was necessary. Descriptive quantitative data were expressed as means $\pm$ standard deviation and qualitative data were expressed as numbers and percentages. Fisher's exact test or χ^2 test was used to perform the between-group comparisons. The prolonged time of chemotherapy was used Mann–Whitney's U test or independent sample t-test to perform the between-group comparisons. Efficacy analysis was based on the intention-to-treat population, defined as all randomized patients who received at least one dose of medication and had at least one efficacy assessment. Delayed chemotherapy and dose reduction analyses were calculated in the per-protocol set (PPS), which defined patients who fulfilled the inclusion/exclusion criteria and completed the treatment regimen. Other efficacy analyses were performed for patients in the full analysis set (FAS), which was defined as all randomized patients who received at least one dose of medication and had at least one efficacy assessment. Safety assessment was calculated in the safety analysis set (SAS). Two-sided p values were reported and p values <0.05 were considered significant. Statistical analyses were performed by using Software SAS 9.4 (SAS Institute).

RESULTS

Patient characteristics

Between January 2019 and July 2021, 166 patients were screened and 148 were randomized into treatment ($n = 94$) or control groups ($n = 54$) (Figure 1). A total of 130 patients were included in the FAS population and SAS population

(treatment group, $n = 87$; control group, $n = 43$). Seven patients assigned to the treatment group and 11 assigned to the control group were excluded, mainly because they did not meet the eligibility criteria or were not evaluated for efficiency. A total of 122 patients were included in the PPS population. Eight patients were excluded because of withdrawal from the study (treatment group, $n = 7$; control group, $n = 1$). Baseline characteristics are described in Table 1. The two groups were well balanced for age, gender, KPS scores, disease stage, vital signs (including leukocyte count, neutrophil count, hemoglobin, and platelet count), and disease history (all $p > 0.05$).
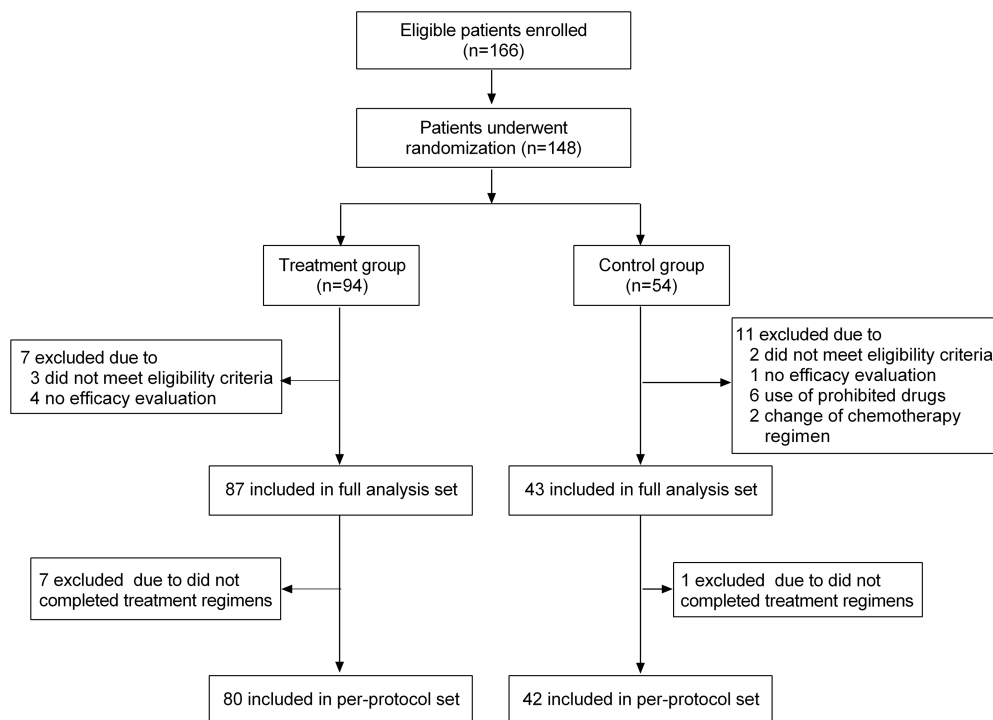
Efficacy

Throughout the study, PEG-rhG-CSF showed superiority in terms of grade 3/4 neutropenia, compared with the control group (1.15% vs. 11.63%, $p < 0.05$). In cycle 1 of chemotherapy, the incidence of grade 3/4 neutropenia in the treatment group was slightly smaller than that of the control group (1.15% vs. 9.30%, $p > 0.05$). In cycle 2, no patients experienced grade 3/4 neutropenia in the treatment group compared to four patients (4/43, 9.52%) in the control group ($p < 0.05$). In cycle 3, grade 3/4 neutropenia was not observed in the two groups (Table 2). In addition, the mean duration of grade 3/4 neutropenia in the treatment group and control group was 2.00 and 3.75 ± 2.47 days, respectively ($p > 0.05$).

During the treatment period, FN occurred in one patient in the control group, but in none of the patients in the treatment group ($p > 0.05$). There was no difference between the treatment group and control group in the delay rate of chemotherapy (43.75% vs. 54.76%), the mean prolonged time of chemotherapy (7.40 ± 6.63 days vs. 10.13 ± 7.59 days) and antibiotics use (0 vs. 4.65%, all $p > 0.05$). The subgroup analysis of FN risk was also performed based on the chemotherapy regimens, including docetaxel+platinum (DP), paclitaxel+platinum (TP), pemetrexed+platinum (AP), and gemcitabine+platinum (GP). The results showed that only one patient who received DP regimen in the control group experienced FN. Moreover, a total of 6 patients in the control group were treated with rhG-CSF at a dose of 100 μg/day in one cycle and 150 μg/day in the other six cycles.

AEs

The summary of AEs is listed in Table 3. Overall, AEs were reported in 41 patients in the treatment group and 21 patients in the control group. The most common AEs reported in this study were anemia (22.99%, 20/87 vs. 34.88%, 15/43) and thrombocytopenia (26.44%, 23/87 vs. 13.95%, 6/43). Fifteen AEs (treatment group: $n = 4$; control group: $n = 11$) were reported as grade 3–4. The rate of neutropenia and leucocyte count decreased in the treatment group was significantly lower than that in the control group

FIGURE 1 Patients flowchart

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                    ┌─────────────────────────────┐
                    │  Eligible patients enrolled  │
                    │         (n=166)              │
                    └─────────────────────────────┘
                                  │
                    ┌─────────────────────────────┐
                    │   Patients underwent         │
                    │   randomization (n=148)      │
                    └─────────────────────────────┘
                         │                    │
              ┌──────────────────┐   ┌──────────────────┐
              │ Treatment group  │   │  Control group   │
              │     (n=94)       │   │     (n=54)       │
              └──────────────────┘   └──────────────────┘
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7 excluded due to
  3 did not meet eligibility criteria
  4 no efficacy evaluation

11 excluded due to
  2 did not meet eligibility criteria
  1 no efficacy evaluation
  6 use of prohibited drugs
  2 change of chemotherapy
    regimen

87 included in full analysis set

43 included in full analysis set

7 excluded due to did not completed treatment regimens

1 excluded due to did not completed treatment regimens

80 included in per-protocol set

42 included in per-protocol set

($p < 0.05$). Other AEs were no statistical difference between the two groups (all $p > 0.05$). The majority of reported AEs were considered mild or moderate (grade 1–2), and there were no serious AEs. Dose reduction was reported in four patients (treatment group: $n = 3$, control group, $n = 1$).

DISCUSSION

In the present study, a randomized controlled trial was conducted to evaluate the efficacy and safety of PEG-rhG-CSF in preventing neutropenia during chemotherapy of NSCLC. The results demonstrated that the administration of primary prophylactic PEG-rhG-CSF significantly reduced the incidence of grade 3/4 neutropenia and FN induced by chemotherapy. No patients who received prophylactic PEG-rhG-CSF experienced FN. In addition, PEG-rhG-CSF also reduced the delay rate of chemotherapy and shortened the prolonged time of chemotherapy.

Neutrophils have been described as potent cytotoxic effectors, for producing many cytotoxic molecules, and exerting direct tumoricidal activity.[19] Furthermore, the incidence and duration of grade 3/4 neutropenia are considered to be the main factors affecting the risk of infection after chemotherapy.[7,20] G-CSF is the major treatment option for chemotherapy-related neutropenia, which has been associated with multiple immune effects, including the stimulation of neutrophil-mediated cytotoxicity of lymphoma cells. Findings from a previous study in patients with cervical cancer receiving chemoradiotherapy demonstrated that prophylaxis with PEG-rhG-CSF was more effective than rhG-CSF in reducing the incidence of grade 3/4 neutropenia (10%

vs. 77.78%).[21] Therefore, our data are consistent with the results of PEG-rhG-CSF used in patients with cervical cancer. In the present study, patients treated with PEG-rhG-CSF (a long-acting form of G-CSF) had a lower incidence and duration of grade 3/4 neutropenia compared to the control group. Holmes et al.[22] presumed constant stimulation of neutrophils and neutrophil precursors in bone marrow and blood may play a role in the improved efficacy noted. Furthermore, PEG-rhG-CSF was administrated once per cycle, which has advantages over rhG-CSF because of the convenience of clinical management and perhaps good patient compliance.

In clinical practice, FN is a potentially life-threatening complication of cancer chemotherapy.[23] Evidence has shown that patients with FN have an increased risk of death, and require immediate hospitalization and intravenous administration of antibiotics when FN occurs.[24] According to the guidelines of the American Society of Clinical Oncology (ASCO),[25] the primary prophylactic G-CSF is recommended by ASCO for the patients who received the FN-high-risk regimen, which was reported to induce FN in 20% or more. In the present study, there was no clear restriction on whether patients received chemotherapy regimens with low, intermediate or high FN risk. Interestingly, all patients in our study received FN-intermediate-risk regimens (DP and TP therapy regimens)[26] or the FN-low-risk regimens (AP and GP therapy regimens).[25,27] Furthermore, there was no statistical difference in the therapy regimens (intermediate-risk and low-risk therapy regimen) between the two groups (all $p > 0.05$). No patients received FN-high-risk regimens. Evidence has reported that FN-low-risk regimens had a lower probability of FN risk (AP, 0–1.3%; GP,

TABLE 1 Baseline characteristics of included patients

Characteristics	Treatment group ($n = 87$)	Control group ($n = 43$)	p value
Age (y, mean $\pm$ SD)	59.06 $\pm$ 7.44	59.70 $\pm$ 7.21	0.64
Gender (n, %)			0.81
Male	54 (62.07)	26 (60.47)	
Female	33 (37.93)	17 (39.53)	
Weight (kg, mean $\pm$ SD)	66.98 $\pm$ 10.85	67.22 $\pm$ 11.27	0.91
Chemotherapy regimen (n, %)			
FN-intermediate-risk regimens			0.70
DP	5 (5.75)	4 (9.30)	
TP	12 (13.79)	7 (16.28)	
FN-low-risk regimens			0.47
AP	64 (73.56)	27 (62.79)	
GP	6 (6.90)	5 (11.63)	
Medical history (n, %)[a]			0.16
Yes	42 (48.84)	15 (35.71)	
No	44 (51.16)	27 (64.29)	
Disease stage (n, %)[b]			0.49
I	23 (29.87)	11 (34.38)	
II	31 (40.26)	8 (25.00)	
III	18 (23.38)	10 (31.25)	
IV	5 (6.49)	3 (9.38)	
Karnofsky performance scores (n, %)[c]			0.34
70	1 (1.64)	1 (4.00)	
80	3 (4.92)	1 (4.00)	
90	57 (93.44)	22 (88.00)	
100	0	1 (4.00)	
Leukocyte count ($\times 10^3$/μL, mean $\pm$ SD)	6.95 $\pm$ 2.32	6.51 $\pm$ 1.98	0.27
Neutrophil count ($\times 10^3$/μL, mean $\pm$ SD)	5.17 $\pm$ 6.31	4.00 $\pm$ 1.64	0.16
Hemoglobin (g/dL, mean $\pm$ SD)	135.98 $\pm$ 14.85	132.82 $\pm$ 12.17	0.092
Platelet count ($\times 10^4$/μL, mean $\pm$ SD)	239.19 $\pm$ 70.11	263.95 $\pm$ 83.34	0.16

Abbreviations: AP, pemetrexed + platinum; DP, docetaxel + platinum; FN, febrile neutropenia; GP, gemcitabine + platinum; SD, standard deviations; TP, paclitaxel + platinum.
[a]The number of patients with missing medical history mising in treatment group and control group was 1 and 1, respectively.
[b]The number of patients with missing disease stage in treatment group and control group was 10 and 11, respectively.
[c]The number of patients with missing karnofsky performance scores missing in treatment group and control group was 26 and 18, respectively.

TABLE 2 Summary of incidence of 3/4 neutropenia for all cycles

Cycle	Treatment group ($n = 87$)	Control group ($n = 43$)	p value
1[a]	1 (1.15)	4 (9.30)	0.074
2[b]	0 (0)	4 (9.52)	0.023
3[c]	0 (0)	0 (0)	–

Note: Data were expressed as n (%).
[a]The number of patients who receive the chemotherapy in cycle 1 in treatment group and control group was 87 and 43, respectively.
[b]The number of patients who receive the chemotherapy in cycle 2 in treatment group and control group was 80 and 42, respectively.
[c]The number of patients who receive the chemotherapy in cycle 3 in treatment group and control group was 4 and 0, respectively.

0–3.7%).[28–32] In our study, no FN was experienced in patients who received the FN-low-risk regimens after the prophylactic use of PEG-rhG-CSF. However, it is unclear whether the above result was caused by the chemotherapy regimen itself or the prophylactic use of PEG-rhG-CSF. Moreover, according to the NCCN Clinical Practice Guidelines in Oncology,[26] FN-intermediate-risk regimens had an FN incidence of 10%–20% in patients with NSCLC. The prophylactic use of CSF had been approved to reduce the risk of FN in FN-intermediate-risk regimens to 0%–13.9%.[8,21,33] Consistent with the prior study, no patients who received FN-intermediate-risk regimens with PEG-rhG-CSF prophylactic

TABLE 3 Summary of adverse events of any grades

Adverse event (n, %)	Treatment group (n = 87)			Control group (n = 43)			p value
	Any grade	Grade 1/2	Grade 3/4	Any grade	Grade 1/2	Grade 3/4	
Any grade	41 (47.13)	37 (42.53)	4 (4.60)	21 (48.84)	14 (32.56)	7 (16.28)	0.854
Leukocyte count decreased	4 (4.60)	4 (4.60)	0 (0.00)	11 (25.58)	8 (18.60)	3 (6.98)	0.001
Anemia	20 (22.99)	20 (22.99)	0 (0.00)	15 (34.88)	15 (34.88)	0 (0.00)	0.15
Thrombocytopenia	26 (29.89)	23 (26.44)	3 (3.45)	7 (16.28)	6 (13.95)	1 (2.33)	0.094
Neutrophil count decreased	4 (4.60)	3 (3.45)	1 (1.15)	9 (20.93)	4 (9.30)	5 (11.63)	0.009
Alanine aminotransferase increased	1 (1.15)	1 (1.15)	0 (0.00)	1 (2.33)	1 (2.33)	0 (0.00)	1.00
Febrile neutropenia	0 (0.00)	0 (0.00)	0 (0.00)	1 (2.33)	0 (0.00)	1 (2.33)	0.33
Pulmonary infections	0 (0.00)	0 (0.00)	0 (0.00)	1 (2.33)	0 (0.00)	1 (2.33)	0.31
Conjunctival calculus of both eyes	1 (1.15)	1 (1.15)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1.00
Aspartate aminotransferase increased	1 (1.15)	1 (1.15)	0 (0.00)	1 (2.33)	1 (2.33)	0 (0.00)	1.00

support experienced FN in our study, suggesting that the prophylactic use of primary PEG-rhG-CSF could also be effective to reduce the risk of FN in FN-intermediate-risk regimens. However, further study will be required to validate these findings in patients with NSCLC. In addition, there was also no statistical difference in the prolonged time of chemotherapy and the delay rate of chemotherapy between the two groups. However, the prolonged time of chemotherapy was shorter in the treatment group compared to the control group. Overall, our results suggest that PEG-rhG-CSF can provide significant clinical benefit as a prophylaxis in patients with NSCLC who are receiving multiple cycles of chemotherapy.

According to a previous study,[14] the AEs associated with PEG-rhG-CSF include erythema (66.70%), bone pain (58.30%), muscle pain (41.70%), headache (25.00%), aspartate aminotransferase (25.0%), fever (16.70%), and thrombocytopenia (8.30%). In the present study, the most common AEs of PEG-rhG-CSF in the treatment group were anemia (22.99%) and thrombocytopenia (29.89%). At baseline, although there were no statistical differences in hemoglobin levels and platelet counts between the two groups, there were numeric differences. At baseline, patients had relatively higher hemoglobin values (mean values: 135.98 ± 14.85 g/dL vs. 132.82 ± 12.17 g/dL) and relatively lower platelet counts (mean values: $239.19 \pm 70.11 \times 10^4/\mu L$ vs. $263.95 \pm 83.34 \times 10^4/\mu L$) in the treatment group compared with the control group. This may explain why the incidence of anemia was lower and thrombocytopenia was higher in the treatment group compared to the control group. The majority of reported AEs were considered mild or moderate (grade 1–2). In addition, the incidence of AEs is different between the treatment and control groups. Four AEs were observed as grade 3–4 in the treatment group compared to 11 AEs in the control group. There were no unexpected AEs reported in the two groups. Moreover, there were no serious AEs reported. Overall, our study demonstrated the acceptable safety and tolerability of PEG-rhG-CSF.

Although the results of this study were very encouraging, there are several potential limitations. First, patients in

the treatment group received PEG-rhG-CSF for prevention during chemotherapy, and patients in the control group received rhG-CSF when WBC $<2.0 \times 10^9$/L or ANC $<1.0 \times 10^9$/L. Because of the different treatment regimens of the two groups, the trial is open labeled. The lack of blinding might cause considerable bias in specific settings. Second, the patients were only recruited from the Chinese population, potentially limiting the generalizability of findings to the broader population. Third, the duration of grade 3/4 neutropenia in each cycle was not evaluated in the present study. Finally, limited by the follow-up period, only efficacy data were reported for the first three cycles of chemotherapy. Therefore, longer follow-up and a double-blind trial may be warranted to validate the efficacy and safety of PEG-rhG-CSF in the prevention of neutropenia caused by multiple cycles of chemotherapy in patients with NSCLC.

CONCLUSION

The present study shows that primary prophylactic treatment with PEG-rhG-CSF could reduce the incidence of neutropenia in patients with NSCLC during multiple cycles of chemotherapy. PEG-rhG-CSF can effectively reduce the occurrence of grade 3/4 neutropenia, FN, and delay chemotherapy in patients with NSCLC, with acceptable safety and tolerability. Our study provides a basis for the clinical application of control neutropenia during multiple cycles of chemotherapy in patients with NSCLC.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT
All data generated or analyze during this study are included in this published article.

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