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8MW0511, a novel, long-acting granulocyte-colony stimulating factor fusion protein for the prevention of chemotherapy-induced neutropenia: final results from the phase III clinical trial

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Abstract

Background 8MW0511 is a novel, long-acting recombinant human granulocyte-colony stimulating factor (G-CSF) produced by the fusion of the N-terminus of highly active modified G-CSF with the C-terminus of human serum albumin (HSA). Current G-CSF treatments require frequent administration and have limitations in efficacy and convenience, highlighting the need for a longer-acting alternative with fewer injections and improved outcomes. Here, we report a phase III study comparing the efficacy and safety of 8MW0511 with those of the approved PEG-rhG-CSF.

Methods Patients with breast cancer were randomized at a 2:1 ratio to receive either 8MW0511 or PEG-rhG-CSF after four cycles of standard chemotherapy with docetaxel and cyclophosphamide, with or without doxorubicin. The primary efficacy endpoint was to evaluate the duration of severe neutropenia (DSN) between 8MW0511 and PEG-rhG-CSF during the first cycle.

Results Eligible patients were enrolled and randomly assigned to receive either 8MW0511 (n = 328) or PEG-rhG-CSF (n = 164). During the first cycle, the average DSN was 0.24 days for the 8MW0511 group and 0.25 days for the PEG-rhG-CSF group. The mean difference in DSN [-0.02 days (95% Confidence interval: -0.12, 0.08)] met the primary study endpoint. During cycles 2–4, the DSN results were consistent with those of cycle 1. The incidence of grade 4 neutropenia was lower in the 8MW0511 group than in the PEG-rhG-CSF group across all chemotherapy cycles. The incidence

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of febrile neutropenia (FN) across all cycles showed no significant difference between the two groups. Other efficacy endpoints and adverse events were comparable between the two groups.

Conclusions The study findings confirm that 8MW0511 is not inferior to PEG-rhG-CSF in terms of efficacy and shows comparable safety profiles. Additionally, 8MW0511 has the potential to significantly decrease the duration of chemotherapy-induced neutropenia, along with a reduction in the occurrence of FN and severe neutropenia.

Keywords Neutropenia, 8MW0511, Breast cancer, Chemotherapy, PEG-rhG-CSF

Background

Neutropenia is the most common hematological toxicity among patients undergoing cancer treatment. Severe depletion of neutrophils increases the risk of invasive infections, which can rapidly progress to serious complications, such as sepsis, septic shock, or even death. These outcomes often result in prolonged hospital stays, the use of broad-spectrum antibiotics, and increased treatment costs. Febrile neutropenia (FN), the most common clinical manifestation of neutropenia, is characterized by severe neutropenia accompanied by fever [1]. FN can lead to dose reductions or delays in chemotherapy regimens, ultimately compromising the efficacy of antitumor treatment. In addition, the elevated risk of infection and mortality following FN necessitates antibiotic treatment, which increases the risk of drug resistance.

Several guidelines emphasize that whether the goal of treatment is cure, prolongation of survival, or improvement of disease-related symptoms, patients receiving high-risk chemotherapy regimens for FN should be treated with granulocyte-colony stimulating factor (G-CSF) prophylaxis 24 h after the first dose of myelosuppressive chemotherapy [2–4]. G-CSF is currently the only safe and effective drug for the prevention and treatment of neutropenia caused by antitumor therapy. Currently, two types of G-CSF are approved for clinical use: short- and long-acting G-CSF. PEG-G-CSF, the most commonly used long-acting drug, has a prolonged half-life, making it convenient for clinical use and the preferred choice for this indication worldwide.

Despite its advantages, PEG-G-CSF has notable limitations due to its complex modification process. These include higher production costs, reduced batch-to-batch stability, and greater difficult quality control. Additionally, because PEG cannot be metabolized by the human body, some problems have been identified with its long-term and high-dose use. For example, animal studies have shown that prolonged high-dose injections of PEG-interferon (PEG-IFNα2a) can cause renal tubular epithelial cell damage in mice [5]. Additionally, a retrospective real-world study showed that PEGylated medicinal products, such as pegfilgrastim and lipegfilgrastim, were associated with a higher incidence of allergic reactions compared to non-PEGylated products, such as filgrastim. The rates of allergic reactions were 1.4 and 5.3 times higher, respectively, for pegfilgrastim and lipegfilgrastim [6].

8MW0511, a new long-acting G-CSF, was developed using albumin fusion platform technology by fusing the N-terminus of highly active recombinant G-CSF with the C-terminus of human serum albumin (HSA). This configuration enhances its affinity for the G-CSF receptor while preserving a high level of activity. The modification significantly reduces the primary pathway of G-CSF metabolism in vivo. Compared to the relatively complex chemical modification process of PEG-G-CSF, 8MW0511 has a simpler production process, lower production costs, and better product homogeneity thanks to its yeast expression system. In previous phase I and phase II studies, we have demonstrated that 8MW0511 is well-tolerated in both health volunteers and breast cancer patients undergoing chemotherapy with a high risk of FN. Based on a comprehensive evaluation of efficacy and safety, as well as PK/PD analysis, a dose of 500 μg/kg is recommended for further study. With a half-life of 34.8 h in patients with breast cancer, 8MW0511 supports single-dose administration per chemotherapy cycle, ensuring efficacy, shortening the duration of neutropenia, and promoting granulocyte recovery.

Here, we present the results of a phase III clinical trial evaluating the efficacy and safety of 8MW0511, compared to PEG-rhG-CSF for the prevention of chemotherapy-induced neutropenia in patients with breast cancer. This trial was approved by the National Medical Products Administration of China and registered at ClinicalTrials.gov (NCT04554056).

Methods

Study design

This randomized, double-blind, multicenter, active-controlled clinical trial included eligible patients who were randomized in a 2:1 ratio into the experiment group (8MW0511 500 μg/kg) or the control group (PEG-rhG-CSF 100 μg/kg). Patients received 8MW0511 or PEG-rhG-CSF via subcutaneous injection on Day 3 of each chemotherapy cycle. All patients received up to four cycles of standard TC or TAC chemotherapy (TC: Docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2; TAC: Docetaxel 75 mg/m^2, doxorubicin 50 mg/m^2 and

cyclophosphamide 500 mg/m^2) administered by intravenous infusion on Day 1 of each cycle.

Participants

The key inclusion criteria were as follows: females aged 18 to 70 years; patients with histologically confirmed breast cancer: patients with early breast cancer who had not received chemotherapy or those with advanced breast cancer who had not received chemotherapy for recurrent or metastatic disease and relapsed more than 1 year after completing adjuvant chemotherapy; body weight $\geq$ 45 kg; planned treatment with standard TC or TAC chemotherapy; Eastern Cooperative Oncology Group (ECOG) performance status $\leq$ 1; life expectancy of at least 3 months; adequate organ and hematologic function defined as follows: absolute neutrophil count (ANC) $\geq 2.0\times10^9$/L, platelet count (PLT) $\geq 100\times10^9$/L, hemoglobin $\geq$ 90 g/L, white blood cell count $\geq 4.0\times10^9$/L, total bilirubin (TBil) $\leq 1.5\times$ upper limit of normal (ULN), alanine transaminase (ALT), and aspartate transaminase (AST) $\leq 1.5\times$ ULN; voluntary participation in the clinical trial, with the ability to provide written informed consent.

The key exclusion criteria were as follows: history of other malignancies; primary hematological disorders; confirmed or suspected central nervous system metastases based on clinical manifestations; history of bone marrow and/or stem cell transplantation; uncontrolled infection or systemic anti-infective treatment within 72 h before randomization into this study; severe chronic disease affecting the renal, liver, heart or other major organs, or poorly controlled diabetes; concomitant diseases that significantly compromise patient safety or interfere with the patient's ability to complete the trial; participation in other clinical trials within 4 weeks of enrolment; planned surgery within 2 weeks or radiotherapy within 4 weeks before chemotherapy; previous cumulative doses of doxorubicin equal to or greater than 150 mg/m^2 (TAC chemotherapy regimen only); pregnant or breastfeeding women; and those considered unsuitable by the researchers.

Endpoints

The primary efficacy endpoint was to evaluate the duration of severe neutropenia (DSN) during the first cycle. Severe neutropenia, corresponding to grade 4 neutropenia according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0, was defined as an ANC $< 0.5\times10^9$/L.

The secondary efficacy endpoints were as follows: (1) duration of grade 4 neutropenia in cycles 2–4, (2) incidence of grade 4 neutropenia across all cycles, (3) incidence of grade 3 or 4 neutropenia across all cycles, (4) duration of grade 3 or 4 neutropenia across all cycles; and (5) incidence of FN across all cycles.

Safety evaluation indicators included the frequency, type, and severity of treatment-emergent adverse events (AEs), clinical laboratory values, physical examination, ECOG, vital signs examination, and immunogenicity.

Procedures

The ANC results were monitored on Day 3 (pre-dose) and Days 5–11 during cycle 1 and on Day 5 and Days 7–11 in cycles 2–4. Once the ANC was observed to decrease to a minimum, daily CBCs were required until the ANC recovered to $\geq 2.0\times10^9$/L.

Before starting the next cycle of chemotherapy, patients needed to meet the following criteria: ANC $\geq 2.0\times10^9$/L, PLT $\geq 100\times10^9$/L, TBil $\leq 1.5\times$ ULN, ALT, and AST $\leq 1.5\times$ ULN. If these criteria were not met, a 14-day waiting period was allowed for recovery. If the criteria were still not met after the waiting period, the participants would not proceed to the subsequent study phase.

All AEs were recorded from the time of study drug administration until 28 days (±7 days) after the last chemotherapy dose. AEs were reported and graded according to NCI-CTCAE version 5.0.

Blood samples for immunogenicity tests were collected at the following time points: before chemotherapy in cycle 1, Day 14 in cycle 1, Day 21 in cycle 2, 28 days after chemotherapy in cycle 4, and at premature withdrawal.

Statistical analysis

Efficacy analyses were conducted for the full analysis set (FAS) and per-protocol set (PPS). Safety analyses were performed using the safety set (SS). The FAS included all randomized participants who received at least one dose of the study drug. The PPS included all participants from the FAS with medication adherence between 80 and 120% and excluded those with protocol deviations that could significantly affect the efficacy analysis. The SS included all participants who were randomized, received at least one dose of any study drug, and had recorded data for safety indicators.

This study was designed as a non-inferiority trial. We compared the mean DSNs of cycle 1 between the study groups using an analysis of covariance. Non-inferiority of 8MW0511 compared to PEG-rhG-CSF was determined by calculating the difference in least squares means (LS means) with its associated 95% confidence interval (CI). Non-inferiority was concluded if the upper bound of the two-sided 95% CI was below the pre-specified non-inferiority margin of 1.0 day. Subgroup analyses were conducted based on the group, chemotherapy regimen (TC vs. TAC), and breast cancer stage (early vs. advanced) to assess the primary efficacy endpoints. For secondary

efficacy endpoints, statistical descriptions were provided based on data characteristics, but p-values for comparisons between groups were not reported. All statistical analyses were performed with SAS (version 9.4).

Results

Patients

Between November 12, 2021, and November 21, 2022, 496 patients with breast cancer from 39 sites in China were enrolled and randomized into this study (8MW0511, n = 331; PEG-rhG-CSF, n = 165) (Fig. 1). A total of 492 patients were included in the FAS: 328 in the 8MW0511 group and 164 in the PEG-rhG-CSF group. The PPS included 322 patients in the 8MW0511 group and 159 patients in the PEG-rhG-CSF group. The SS set was identical to the FAS. Because the PPS results were broadly consistent with those of the FAS, only the FAS results are presented here for simplicity.

All patients were female, with a median age of 51.5 years and a mean weight of 61.9 ± 9.7 kg. Seventy-nine percent had early-stage breast cancer, whereas 21% had advanced-stage breast cancer. The TC regimen accounted for approximately 62%, and the TAC regimen accounted for approximately 38% of the randomized chemotherapy regimens. The two groups were well-balanced in terms of demographics and baseline disease characteristics, as shown in Table 1.

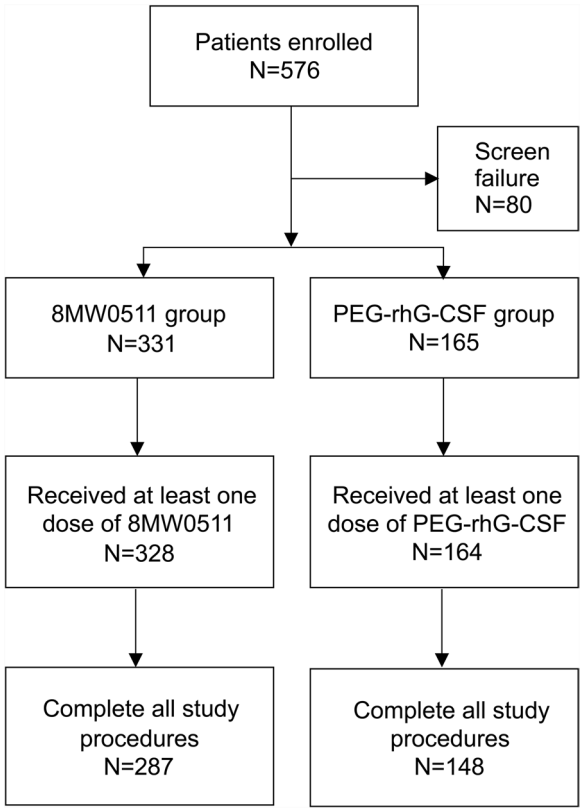

Fig. 1 Patient disposition

Efficacy

The DSN in different cycles

During cycle 1, the average DSN was 0.24 ± 0.580 days for the 8MW0511 group and 0.25 ± 0.558 days for the PEG-rhG-CSF group. The average difference in DSN was -0.02 ± 0.051 (95%CI -0.12, 0.08), and the upper bound of the two-sided 95% CI was below the non-inferiority margin of 1.0 day, demonstrating that 8MW0511 is non-inferior to the reference drug. During cycles 2–4, the average DSN results were consistent with those of cycle 1. Particularly in cycle 2, the 8MW0511 group exhibited a slightly lower average DSN than the PEG-rhG-CSF group, with an average difference in DSN of -0.09 ± 0.032 (95%CI -0.15, -0.03). Subgroup analysis based on cancer

Table 1 Patients' characteristics

Characteristic	8MW0511 (N = 328)	PEG-rhG-CSF (N = 164)	Total (N = 492)
Age, years			
Median	51.0	52.0	51.5
Min, Max	27, 70	26, 70	26, 70
Sex, N(%)			
Female	328 (100.0)	164 (100.0)	492 (100.0)
Height(cm)			
Mean ± SD)	158.7 ± 5.5	158.5 ± 5.1	158.6 ± 5.4
Min, Max	140,176	143,172	140,176
Weight(kg)			
Mean ± SD	62.1 ± 9.6	61.7 ± 10.1	62.0 ± 9.7
Min, Max	45, 112	46, 123.7	45, 123.7
Body areas(m^2)			
Mean ± SD	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1
Min, Max	1.3, 2.2	1.3, 2.3	1.3, 2.3
Cancer stage, N(%)			
early	257 (78.4)	131 (79.9)	388 (78.9)
advanced	71 (21.6)	33 (20.1)	104 (21.1)
Metastasis, N(%)			
Yes	152 (46.3)	75 (45.7)	227 (46.1)
No	176 (53.7)	89 (54.3)	265 (53.9)
Baseline ANC, (10^9/L)			
Mean ± SD	4.14 ± 1.49	4.16 ± 1.63	4.14 ± 1.53
Min, Max	2.02, 12.91	2.04, 11.58	2.02, 12.91
Chemotherapy, N(%)			
TC	204 (62.2)	101 (61.6)	305 (62.0)
TAC	124 (37.8)	63 (38.4)	187 (38.0)

stage and chemotherapy regimen revealed similar average DSN values for both groups in cycle 1 (Table 2).

Incidence of neutropenia

There were no differences in the incidences of grade 4 and grade 3 or 4 neutropenia between the two groups. However, a lower incidence was observed in the 8MW0511 group across all chemotherapy cycles. A significant decrease in the incidence of grade 4 and grade 3 or 4 neutropenia was observed in cycles 2–4 for both groups, with a more pronounced decrease in the 8MW0511 group (Table 2).

Incidence of FN

The incidence of FN across all cycles was low and not significantly different between the two groups, with seven patients (2.1%) in the 8MW0511 group and six patients (3.7%) in the PEG-rhG-CSF group (Table 2).

Pharmacodynamic characteristics

There was no significant difference in the baseline ANC between the two groups. The ANC value in cycle 1 indicated that the time curves exhibited bimodal changes in both groups. The first peak in both groups occurred on day 5 of chemotherapy, showing the greatest change compared to baseline. The ANC value then decreased slowly after day 5, reaching a trough on day 7. The overall trends and ANC changes on days 1–5 were similar in both groups; however, the mean ANC in the 8MW0511 group was slightly higher than that in the PEG-rhG-CSF group after day 5 (Fig. 2).

Safety

Overall, 8MW0511 was well tolerated by patients with breast cancer, with AEs in the 8MW0511 group being consistent with those in the PEG-rhG-CSF group. Most

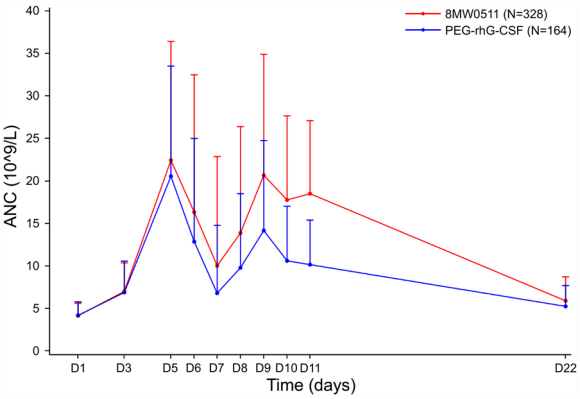

Fig. 2 Mean (+SD) ANC profiles in cycle 1-FAS

Table 2 Efficacy endpoints in the full analysis set (FAS)

	8MW0511 (N = 328)	PEG-rhG-CSF (N = 164)	Difference	95%CI
DSN, days Mean (SD)			LS Mean (SE)	
Cycle 1*	0.24(0.580)	0.25(0.558)	−0.02(0.051)	(−0.12,0.08)
Cycle 2	0.04(0.244)	0.13(0.436)	−0.09(0.032)	(−0.15,-0.03)
Cycle 3	0.04(0.221)	0.08(0.293)	−0.04(0.025)	(−0.09,0.01)
Cycle 4	0.05(0.281)	0.10(0.392)	−0.05(0.032)	(−0.11,0.02)
Incidence of grade 4 neutropenia, n(%)				
Cycle 1	54(16.5)	32(19.5)	−3.05	(−10.17,4.07)
Cycle 2	10(3.0)	16(9.8)	−6.97	(−11.37,-2.56)
Cycle 3	9(2.7)	11(6.7)	−4.19	(−8.19,-0.19)
Cycle 4	11(3.4)	10(6.1)	−2.76	(−6.95,1.43)
Incidence of grade 3/4 neutropenia, n(%)				
Cycle 1	90(27.4)	49(29.9)	−2.44	(−10.88,6.00)
Cycle 2	36(11.0)	28(17.1)	−6.22	(−12.82,0.38)
Cycle 3	31(9.5)	27(16.5)	−7.31	(−13.82,-0.81)
Cycle 4	32(9.8)	25(15.2)	−5.34	(−11.93,1.26)
Incidence of FN, n(%)				
Cycle 1	7(2.1)	5(3.0)	−0.91	(−3.81,1.98)
Cycle 2	0	1(0.6)	−0.64	(−1.52,0.25)
Cycle 3	0	1(0.6)	−0.65	(−1.56,0.26)
Cycle 4	0	0	/	/

* primary efficacy endpoints

participants in this trial experienced at least one treatment-related AE (8MW0511, 97.9%; PEG-rhG-CSF, 97.0%). The incidence of adverse drug reactions (ADRs) was similar in both groups (8MW0511, 48.5%; PEG-rhG-CSF, 48.8%), and the severity of ADRs was mostly grades 1–2 in both groups. The most common ADRs (≥10%) in the 8 MW0511 group were asthenia (18.0%) and bone pain (12.5%). In the PEG-rhG-CSF group, the most common ADR was asthenia (12.8%). Other frequently reported ADRs (≥5%) in the 8MW0511 group included increased alanine aminotransferase (9.5%), pain (8.2%), nausea (7.6%), and increased aspartate aminotransferase (6.1%). In the PEG-rhG-CSF group, frequent ADRs (≥5%) included pain (9.1%), back pain (9.1%), bone pain (8.5%), nausea (7.9%), increased alanine aminotransferase (7.3%), and pain in extremity (6.1%). The incidence of AEs was comparable between the two groups (Table 3).

Musculoskeletal pain and anaphylaxis are common adverse reactions to G-CSF administration. Analysis of grade≥3 ADRs in this trial revealed one case of limb pain and urticaria in the 8MW0511 group, whereas the PEG-rhG-CSF group reported two cases of urticaria, one urticarial vasculitis, one allergic dermatitis, one back pain. No cases of splenic rupture or anaphylactic shock occurred in either group. The incidence of ADRs leading to drug or chemotherapy discontinuation was low and similar between the two groups (both 1.2%). The incidence of ADRs leading to study withdrawal was slightly lower in the 8MW0511 group than in the PEG-rhG-CSF group (0.9% vs. 1.8%). The incidence of serious ADRs was 1.2% in the 8MW0511 group and 2.4% in the PEG-rhG-CSF group. One death due to the progression of brain metastasis was observed in the 8MW0511 group, which was considered unrelated to the study drug by the researchers.

Immunogenicity assays detected anti-drug antibodies (ADA) positivity in both treatment groups. One patient in the 8MW0511 group tested positive for neutralizing antibodies. Further association analysis of ADA-positive data with PK, PD, and safety data revealed no relevant effects.

Discussion

This clinical trial evaluated the efficacy and safety of 8MW0511 compared to a positive control drug in Chinese patients with breast cancer who had received four cycles of TC or TAC chemotherapy. This is the first publication of detailed phase 3 clinical data for 8MW0511. Based on the latest clinical trial guidelines and consensus, the primary efficacy endpoint of this trial was to evaluate the DSN during the first cycle. The results of our study showed no significant difference in the mean DSN between the groups, consistent with the results from cycles 2–4. Throughout the study, most patients did not experience grade 4 neutropenia. Grade 4 neutropenia occurred mainly during cycle 1, and its incidence decreased significantly during cycles 2–4. 8MW0511 and PEG-rhG-CSF were shown to effectively reduce the incidence of grade 4 ANC, with 8MW0511 demonstrating a notably lower effect.

The incidence of FN across all cycles showed no significant difference between the two groups. During the study period, FN was observed in seven cases (2.1%) in the 8MW0511 group and in six cases (3.7%) in the PEG-rhG-CSF group. Notably, no instances of FN were reported in the 8MW0511 group during cycles 2–4, whereas the PEG-rhG-CSF group experienced one case each in the second and third cycles. A low incidence of FN is important in clinical practice, as it reduces the risk of infection and antibiotic use, ensures uninterrupted chemotherapy, improves patient compliance, and decreases hospitalization rates. In our study, 8MW0511 and PEG-rhG-CSF performed well in preventing

Table 3 Adverse events related to the study drug (incidence≥5.0%)

Adverse event	8MW0511 (n=328), n(%)		PEG-rhG-CSF (n=164), n(%)	
	Any grade	Grade≥3	Any grade	Grade≥3
Any event	159(48.5)	9(2.7)	80(48.8)	5(3.0)
Asthenia	59(18.0)	1(0.3)	21(12.8)	0
Pain	27(8.2)	1(0.3)	15(9.1)	0
Bone pain	41(12.5)	0	14(8.5)	0
Back pain	16(4.1)	0	15(9.1)	1(0.6)
Limb pain	10(3.0)	1(0.3)	10(6.1)	0
Nausea	25(7.6)	0	13(7.9)	0
Alanine aminotransferase increased	31(9.5)	1(0.3)	12(7.3)	0
Aspartate aminotransferase increased	20(6.1)	1(0.3)	7(4.3)	0

chemotherapy dose reductions, with no significant difference observed between the two groups.

Safety results indicated that the incidence of ADR with 8MW0511 was 48.5%, and the severity was mainly mild to moderate (Grades 1–2), suggesting it was well tolerated. Asthenia (18.0%) and bone pain (12.5%) were the most common ADRs. There were no significant differences in ADRs compared with PEG-rhG-CSF. Overall, the incidence of serious ADRs was low in both groups (1.1% vs. 2.4%), and all AEs resolved. No deaths were related to the study drugs. Moreover, we did not observe splenic rupture, acute respiratory syndrome, severe allergic reactions, or other potentially serious adverse reactions in our study according to the manufacturer's instructions. However, as our study included only Chinese breast cancer patients and the sample size was limited, it is insufficient to conclusively rule out these safety risks. Therefore, these potential safety concerns warrant further attention in future clinical applications. Bone pain is a common ADR associated with G-CSF; therefore, we focused on bone pain in this study. The incidence of treatment-related bone pain was 12.5% in both groups, with mild severity (Grades 1–2).

We performed further analyses on participants who tested positive for neutralizing antibodies. One patient had preexisting ADA, resulting in pre- and post-dose plasma samples being ADA-positive. The ratio of the post-dose ADA titer to the pre-dose ADA titer was less than two dilutions. According to the industry consensus [7], this kind of ADA positivity was not considered to be related to the study drug. During the study, this patient did not experience any grade 4 neutropenia, serious AEs, or AEs leading to withdrawal.

Although designed as a non-inferiority study, 8MW0511, a long-acting G-CSF, evidently achieved an efficacy similar to that of PEG-rhG-CSF. Particularly, it showed a numerical advantage in terms of the incidence of FN and grade 4 ANC. Furthermore, AEs and serious AEs were comparable between the two groups. This study demonstrates that 8MW0511 can offer clinical benefits to patients with malignant tumors undergoing chemotherapy, particularly those at high risk of FN, in efficacy and safety.

Adjuvant chemotherapy with G-CSF is an effective strategy that not only reduces the risk of grade 4 myelosuppression but also enables patients to receive higher doses of chemotherapy, leading to improved outcomes. The ability of G-CSF to prevent FN can significantly lower the cost of antibiotic use and reduce overall hospitalization duration, which has important pharmacoeconomic implications for patients and society [8].

With advancements in research and pharmaceutical processing, long-acting G-CSF generally has lower risks of FN and FN-related complications than short-acting prophylaxis [9]. In addition, long-acting G-CSF is used for prophylactic and therapeutic purposes [10]. Long-acting G-CSF guarantees not only optimal treatment in traditional chemotherapy but also provides supportive benefits in new cancer therapies, such as targeted drugs and antibody–drug conjugates. Adequate prophylactic supportive treatment ensures sufficient exposure to antitumor drugs. However, given the possibility of drug accumulation and allergy associated with PEG [5, 6], long-term use of PEG-rhG-CSF may also carry uncertain risks. Albumin-modified long-acting G-CSF could reduce the risk of PEG while maintaining efficacy and safety. 8MW0511 meets these clinical needs and provides significant benefits for patients with breast cancer. The development of 8MW0511 will expand the range of G-CSF drugs and offer more options for managing severe neutropenia during chemotherapy. Although the correlation between chemotherapy-induced neutropenia and tumor type may not be significant, this study has certain limitations, as it included only the Chinese breast cancer population.

Conclusions

This phase 3 study demonstrated the non-inferior efficacy and comparable safety of 8MW0511 compared to PEG-rhG-CSF. 8MW0511 has the potential to significantly decrease the duration of chemotherapy-induced neutropenia, along with reducing the occurrence of FN and severe neutropenia. Future studies may focus on collecting clinical data on the use of 8MW0511 in different types of solid tumors to further analyze its efficacy and safety, including results from long-term use.

Abbreviations

G-CSF	Granulocyte-colony stimulating factor
HAS	Human serum albumin
FN	Febrile neutropenia
DSN	Duration of severe neutropenia
ANC	Absolute neutrophil count
PLT	Platelet count
TBil	Total bilirubin
ULN	Upper limit of normal
ALT	Alanine transaminase
AST	Aspartate transaminase
ADA	Anti-drug antibodies
FAS	Full analysis set
PPS	Per-protocol set
SS	Safety set
ADRs	Adverse drug reactions
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events ECOGEastern Cooperative Oncology Group
AEs	Adverse events

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Author contributions
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Availability of data and materials
The datasets generated and/or analyzed during the current study are not publicly available because of pending regulatory submission and approval but may be available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate
This study was approved by the ethics committees of each participating institution. All procedures performed in studies involving participants were in accordance with the ethical standards of the institutional and/or national research committee, and this was outlined in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All patients in this study provided written informed consent before undergoing any study-related procedures.

Consent for publication
Not applicable.

Competing interests
PW, JD, HZ, SL, CZ, SC, and SW reported employment from Mabwell (Shanghai) Bioscience Co, Ltd; employment from the study sponsor (Mabwell [Shanghai] Bioscience Co, Ltd) at the time of study outside the submitted work.

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