

## A randomized double-blind phase II study to evaluate same-day vs next-day pegfilgrastim with carboplatin and docetaxel in patients with NSCLC

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<b>Origin of Study</b>	USA
<b>Type of Study</b>	MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PHASE II STUDY
<b>Objectives</b>	Evaluate whether administration of pegfilgrastim (Neulasta) on the same day as completing chemotherapy using carboplatin and docetaxel (Taxotere) is effective and has a tolerable safety profile when compared with administration approximately 24 hours after completion of chemotherapy for the treatment of advanced non-small cell lung cancer (NSCLC).
<b>Study Design</b>	<p>Patients were randomized to receive either 6 mg of pegfilgrastim within 4 hours of completing chemotherapy with carboplatin (area under the curve 6) and docetaxel (75 mg/m<sup>2</sup>) and placebo 24 hours later (same-day group) or placebo on the same day as chemotherapy and 6 mg of pegfilgrastim 24 hours after completion of chemotherapy (next-day group).</p> <p>A complete blood count (CBC) was obtained during cycles 1 and 4 on day 1 before chemotherapy administration, daily starting on day 5 until absolute neutrophil count (ANC) recovery to <math>&gt; 0.5 \times 10^9/L</math>, and then weekly. CBC also was taken during cycles 2, 3, 5, and 6 on day 1 before chemotherapy administration and then weekly.</p> <p>Oral temperature was followed on a patient diary card whenever the patient felt feverish. If temperature was <math>\geq 38.0^\circ C</math>, oral temperature was collected daily until it dropped below that point. If temperature was <math>\geq 38.2^\circ C</math>, a CBC was scheduled.</p> <p>Patients could not use prophylactic anti-infectives.</p>
<b>Patients</b>	Patients were $\geq 18$ years of age, were diagnosed with stage IIIB or IV NSCLC, and were not treated previously with chemotherapy. In the same-day group (n = 44), 27% were female, and 80% were white (median age, 64 years); in the next-day group (n = 44), 41% were female, and 93% were white (median age, 66 years).
<b>Observations</b>	<p>Patients in both groups had comparable mean baseline ANC levels, and similar proportions of patients completed the study (same-day group, 43%; next-day group, 45%). In cycle 1, 5% of patients in both groups experienced grade 4 neutropenia (mean duration, 0.05 days). In cycle 4, 10% of the same-day group experienced grade 4 neutropenia that lasted for 1 day only (mean duration, 0.1 day); none of those in the next-day group did, however. No patients experienced febrile neutropenia during the study.</p> <p>The incidence of hospitalization across cycles was 45% in the same-day group and 30% in the next-day group. None of the adverse events leading to hospitalization was attributed to neutropenia.</p> <p>In the same-day group, 73% of patients received planned doses on time, 14% had dose reductions only, and 18% had dose delays only; in the next-day group, 68% of patients received planned doses on time, 14% had dose reductions only, and 18% had dose delays only. The mean average relative dose intensity for both groups was 0.98.</p> <p>Serious adverse events were reported by 44% of the same-day group and 33% of the next-day group; these</p>

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events primarily were driven by dyspnea and pneumonia. Other severe adverse reactions were expected for patients given carboplatin and docetaxel; none was considered to be related to pegfilgrastim.

Three patients in the same-day group and four in the next-day group died; none of these deaths was considered to be related to the study drug.

**Conclusions**

No episodes of febrile neutropenia or hospitalization were attributed to neutropenia.

Few patients in both groups experienced dose delays or reductions in chemotherapy delivery.

In cycle 1, the upper limit of the two-sided 95% confidence limit for the difference in mean duration of grade 4 neutropenia was less than the prespecified non-inferiority margin of 2 days, thereby meeting the primary endpoint.

**Discussion**

In patients with NSCLC, combination chemotherapy with carboplatin and docetaxel is active, but this regimen carries a moderate or high risk of febrile neutropenia. In an effort to reduce chemotherapy-induced neutropenia, patients are typically given pegfilgrastim (a long-acting granulocyte colony-stimulating factor) by subcutaneous injection once per cycle on the day after chemotherapy. However, such next-day administration may require that patients make another visit. This noninferiority trial compared the efficacy and safety of same-day pegfilgrastim—a schedule that would be more convenient for patients—with those of next-day pegfilgrastim.

The randomized, double-blind phase II trial was conducted among adult patients with previously untreated stage IIIB or IV NSCLC who were candidates for combination carboplatin and docetaxel chemotherapy. They were assigned in equal numbers to receive 6 mg of pegfilgrastim on the same day as chemotherapy (within 4 hours afterward) or on the next day (about 24 hours afterward).

The rate of grade 4 neutropenia in cycle 1 was only 5% in each group, and the duration of this complication (the trial's primary endpoint) did not differ between groups, with a value of 0 days in each. The rate of grade 4 neutropenia in cycle 4 was 10% in the same-day group (with the complication lasting only 1 day in affected patients) and 0% in the next-day group. None of the patients developed febrile neutropenia. The rate of serious adverse events was 44% with same-day administration and 33% with next-day administration.

The investigators concluded that pegfilgrastim starting in cycle 1 was well tolerated with both the same-day and next-day strategies. "Although the incidence of grade 3/4 neutropenia was lower than previously reported for this [chemotherapy] regimen, the duration of grade 4 neutropenia appeared to be similar for patients in the same-day and next-day groups," they write. "Additionally, few patients experienced reductions or delays in chemotherapy delivery."

**Key Points**

- Duration of severe neutropenia was similar in patients receiving pegfilgrastim on the same day or the next day of chemotherapy.
- Use of pegfilgrastim from the first cycle was well tolerated in NSCLC patients receiving carboplatin and docetaxel.
- Due to the lack of neutropenic events, no conclusions regarding the relative efficacy of same-day versus next-day pegfilgrastim use may be drawn. Thus, pegfilgrastim should be administered approximately 24 hours after completion of chemotherapy.

**Reference**

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