

## Pegfilgrastim Supports Dose-Dense Carboplatin/Vinorelbine in the Treatment of Thoracic Malignancies

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<b>Origin of Study</b>	USA
<b>Type of Study</b>	PHASE II, OPEN-LABEL PROSPECTIVE CLINICAL TRIAL
<b>Objectives</b>	Assess the efficacy and safety of pegfilgrastim for decreasing the incidence of febrile neutropenia in patients with thoracic malignancies receiving dose-dense chemotherapy
<b>Study Design</b>	<p>Chemotherapy-naïve patients with non-small cell lung cancer or other thoracic malignancies, including mesothelioma, were treated with a dose-dense regimen of carboplatin (AUC 6 mg/mL/min) on day 1 and vinorelbine (30 mg/m<sup>2</sup>) on days 1 and 8 of an every-3-week dosing schedule, for a total of 4 planned cycles.</p> <p>Pegfilgrastim was administered on day 9 as a single 6-mg subcutaneous injection and repeated each cycle.</p> <p>The primary endpoint was the incidence of febrile neutropenia in cycle 1.</p> <p>Secondary endpoints included the incidence of grade 3/4 neutropenia and thrombocytopenia, grade 2–4 anemia, nonhematologic toxicity, and adverse events across all treatment cycles.</p>
<b>Patients</b>	<p>Twenty-seven of 30 planned patients were enrolled at the time this interim analysis was reported (August 2003). Data were available on 23 patients (15 men and 8 women) who completed a total of 62 patient cycles.</p> <p>Patients had good performance status (PS ≤ 2), a median age of 64 years, a mean baseline hemoglobin value of 13.1 g/dL, a mean baseline platelet count of 287 × 10<sup>9</sup>/L, and a mean baseline absolute neutrophil count (ANC) of 5.9 × 10<sup>9</sup>/L.</p>
<b>Observations</b>	<p>There were no reported episodes of febrile neutropenia.</p> <p>Hematologic toxicities included nine instances of moderate to severe anemia (eight grade 2 and one grade 3), one case of severe (grade 3) thrombocytopenia, and six cases of severe neutropenia (four grade 3 and two grade 4).</p> <p>Reduction in chemotherapy dose intensity was required for 10 patients: half of them for non-hematologic toxicities and half for hematologic toxicities (one case of grade 3 neutropenia and four cases of grade 2 neutropenia).</p> <p>Across all patient cycles, mean hematologic nadirs included a hemoglobin nadir of 11.2 g/dL, platelet nadir of 142 × 10<sup>9</sup>/L, and ANC nadir of 3.6 × 10<sup>9</sup>/L.</p> <p>The most common adverse event related to pegfilgrastim administration was bone pain.</p>
<b>Conclusions</b>	Pegfilgrastim provides effective protection from febrile neutropenia in the current chemotherapy regimen. To better maintain dose density and further reduce neutropenia, pegfilgrastim administration on day 2 of each cycle warrants investigation.

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### Discussion

This phase II study shows that pegfilgrastim (Neulasta) protects against febrile neutropenia in a dose-dense chemotherapy regimen for lung cancer and other thoracic malignancies. Previously, dose-dense chemotherapy had been shown to improve outcomes in lymphoma and breast cancer, but studies of dose-dense chemotherapy in lung cancer were limited.

The investigators evaluated the use of pegfilgrastim support in the treatment of patients with thoracic malignancies undergoing a dose-dense carboplatin (Paraplatin)/vinorelbine regimen. The study included patients with previously untreated non-small cell lung cancer, mesothelioma, or other thoracic malignancies.

Treatment included an every-3-week regimen with carboplatin (AUC 6 mg/mL/min) on day 1 and vinorelbine (30 mg/m<sup>2</sup>) on days 1 and 8. Patients received pegfilgrastim as a 6-mg subcutaneous injection on day 9 of each of 4 planned cycles. The primary endpoint of this trial is incidence of febrile neutropenia in cycle 1, with secondary endpoints of grade 3/4 myelosuppression, anemia, nonhematologic toxicity, and adverse events.

A total of 30 patients were planned in the study. Riedel and colleagues reported on 23 patients who, at the time of this report, had completed a total of 62 chemotherapy cycles. This patient group included 15 men and 8 women (median age, 64 years) with good performance status.

At baseline, the mean ANC was  $5.9 \times 10^9/L$ , mean baseline platelet count was  $287 \times 10^9/L$ , and mean hemoglobin level was 13.1 g/dL. During chemotherapy, mean hematologic nadirs included an ANC of  $3.6 \times 10^9/L$ , platelet count of  $142 \times 10^9/L$ , and hemoglobin level of 11.2 g/dL across all chemotherapy cycles. Bone pain was the most commonly reported adverse event.

No episodes of febrile neutropenia were seen. Anemia occurred in nine cases (eight grade 2, one grade 3), neutropenia in six cases (four grade 3, two grade 4), and grade 3 thrombocytopenia in one case. Ten patients required dose reduction, half for hematologic toxicities, mostly grade 2 neutropenia.

These results suggest that pegfilgrastim, given on day 9 of a dose-dense chemotherapy regimen for thoracic malignancies, protects against febrile neutropenia. Pegfilgrastim on day 2 of each chemotherapy cycle may also be investigated.

### Key Points

- Pegfilgrastim protects against febrile neutropenia in a dose-dense chemotherapy regimen for lung cancer and other thoracic malignancies.
- There were no episodes of febrile neutropenia in 23 patients completing a total of 62 cycles of dose-dense carboplatin/vinorelbine therapy.
- Bone pain was the most common adverse effect of pegfilgrastim reported.

### References

Riedel RF, Garst J, Dunphy F, et al. Pegfilgrastim supports dose-dense carboplatin/vinorelbine in the treatment of thoracic malignancies. Poster presented at the 10th World Conference on Lung Cancer; August 10–14, 2003; Vancouver, BC. Abstract P-683.