

Pegfilgrastim provides effective primary prophylaxis against febrile neutropenia in patients with non-Hodgkin's lymphoma undergoing chemotherapy: initial results from an integrated analysis—the Neulasta Versus Current Neutropenia Management Practice (NEUCUP) Project

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Origin of Study	United Kingdom, Germany, Switzerland, USA
Type of Study	RETROSPECTIVE INTEGRATED ANALYSIS
Objectives	Evaluate the safety and efficacy of prophylactic pegfilgrastim (Neulasta) in a large non-Hodgkin's lymphoma (NHL) population.
Study Design	<p>Investigators evaluated data from three prospective trials to assess the efficacy and safety of primary pegfilgrastim prophylaxis in NHL patients given cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or CHOP-like regimens with or without rituximab (Rituxan); the primary outcome measure was the proportion of patients developing febrile neutropenia.</p> <p>Studies were phase II–IV clinical trials and prospective or retrospective observational studies that were well controlled. They enrolled NHL patients who received 3- or 4-weekly cycles of CHOP or CHOP-like chemotherapy with or without rituximab. Patients received pegfilgrastim from the first cycle. Data on the incidence of febrile neutropenia were collected in this research.</p>
Patients	In all, 282 patients received pegfilgrastim and were included in these analyses.
Observations	<p>Just 15% of patients experienced febrile neutropenia over all cycles; approximately half of these cases occurred during cycle 1.</p> <p>The reported World Health Organization grade 3/4 hematologic toxicities included white blood cell count (WBC) $< 2.0 \times 10^9/L$ (63%), absolute neutrophil count (ANC) $< 1.0 \times 10^9/L$ (67%), hemoglobin level < 8.0 g/dL (8%), platelet count $< 50 \times 10^9/L$ (21%); grade 4 WBC $< 1.0 \times 10^9/L$ was 39%, and ANC $< 0.5 \times 10^9/L$ was 55%.</p> <p>Further, 15% of patients were hospitalized due to a neutropenic event and 11% due to febrile neutropenia. Anti-infectives were prescribed for 60%. Across all chemotherapy cycles, a relative dose intensity (RDI) $\geq 85\%$ was achieved by 88%; an RDI $\geq 90\%$ was achieved by 83%.</p> <p>The study drug was effective against febrile neutropenia in the 172 patients ≥ 65 years of age; febrile neutropenia occurred in 18% of these patients as compared with 13% of younger patients. Hospitalization due to febrile neutropenia occurred in 13% of patients ≥ 65 years of age and 6% of younger patients.</p>
Conclusions	<p>With current management of neutropenia, CHOP-like chemotherapy is linked with febrile neutropenia in 22%–50% of patients.</p> <p>Prophylaxis with pegfilgrastim was associated with a relatively low occurrence of febrile neutropenia and a high proportion of patients achieving an RDI $\geq 90\%$.</p> <p>Pegfilgrastim may have benefits over current neutropenia management in NHL patients given CHOP or CHOP-like regimens, enabling the use of chemotherapy on time and schedule.</p>

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Discussion

CHOP-like regimens used to treat NHL are associated with febrile neutropenia rates of up to 50% with current neutropenia management (Aapro MS et al. *Eur J Cancer* 2006;42:2433–2453; Pettengell R et al. *Haematologica* 2006;91[suppl 1]:69. Abstract 185). Approximately 50% of febrile neutropenia episodes occur during the first cycle of chemotherapy treatment (Lyman G et al. *Leuk Lymphoma* 2003;44:2068–2076). The investigators of this study, therefore, examined the efficacy of the long-acting granulocyte colony-stimulating factor (G-CSF) pegfilgrastim as primary prophylaxis against febrile neutropenia and treatment-related complications in NHL patients receiving CHOP-like regimens. The analysis included 282 patients drawn from three prior studies of pegfilgrastim.

With pegfilgrastim as prophylaxis, the incidence of febrile neutropenia was relatively low for an NHL population. Febrile neutropenia occurred in 16% of all cycles and 7% during the first cycle. For cycles 2 through 6, rates were 1%–4%. Importantly, only 18% of the elderly subset—those at greater risk of chemotherapy-induced neutropenia, dose delays, and hospitalization—experienced febrile neutropenia with pegfilgrastim as primary prophylaxis.

“These initial data suggest that primary prophylaxis with pegfilgrastim may have benefits over current neutropenia G-CSF management in NHL patients receiving CHOP or CHOP-like regimens,” Dr. Pettengell said. “The rate of febrile neutropenia is significantly less than we typically see with standard G-CSF.”

“This enabled the delivery of chemotherapy on time and on schedule,” she said. “In terms of dose reductions and delays, about a quarter of patients were delayed more than 3 days, but only 8% were delayed for more than 1 week. And in almost all patients—83%—the RDI was maintained \geq 90%. I think this is very impressive.

“The other important finding was that patients aged 65 and older, who are at increased risk for febrile neutropenia and hospitalizations, had less risk with pegfilgrastim. Febrile neutropenia was diagnosed in 18%, and 78% received an RDI greater than 90%,” she added. “This is important, because older patients often receive less chemotherapy.”

Key Points

- These data support use of pegfilgrastim as primary prophylaxis against febrile neutropenia and neutropenic complications in NHL patients receiving CHOP-like chemotherapy, particularly the elderly, for whom the risk of febrile neutropenia and hospitalization is greatest.
- These findings support the current American Society of Clinical Oncology/European Organization for Research and Treatment of Cancer guidelines.
- Future studies will examine neutropenia-related outcomes and chemotherapy delivery for primary prophylaxis pegfilgrastim versus current neutropenia management.

Reference

Pettengell R, Skacel T, Aapro M, Duehrsen U, Easton V, Lyman G. Pegfilgrastim provides effective primary prophylaxis against febrile neutropenia in patients with NHL undergoing chemotherapy: initial results from an integrated analysis—the Neulasta Versus Current Neutropenia Management Practice (NEUCUP) Project. Presented at the 48th Annual Meeting of the American Society of Hematology; December 9–12, 2006; Orlando, Florida. Abstract 1150.