

Final results of a large, community-based, prospective study evaluating the impact of first and subsequent cycle pegfilgrastim on neutropenic events in patients receiving myelosuppressive chemotherapy

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Origin of Study	USA
Type of Study	COMMUNITY-BASED, PROSPECTIVE STUDY
Objectives	Assess the impact of first and subsequent cycle pegfilgrastim (Neulasta) use on neutropenic events in patients receiving chemotherapy in community practice.
Study Design	<p>Patients were to receive 6 mg of pegfilgrastim approximately 24 hours after chemotherapy (minimum 4 cycles planned).</p> <p>Investigators examined patients for incidence of grade 3/4 neutropenia, febrile neutropenia, and intravenous antibiotic use.</p>
Patients	<p>Patients were ≥ 18 years of age and had a pathologically confirmed malignancy (except for leukemia or myelodysplastic syndrome) and planned use of at least 4 chemotherapy cycles every 14, 21, or 28 days.</p> <p>In all, 2,112 patients (mean age, 59 years; 75% female) were involved in the final analysis; 36% were at least 65 of years age, 53% had stage 3/4 or extensive disease, 23% received prior chemotherapy, 17% received prior radiotherapy, and 27% had a significant comorbidity.</p> <p>Major tumor types included breast (46%), lung (16%), and ovarian (8%) cancers and lymphoma (18%).</p>
Observations	<p>Febrile neutropenia was experienced by 3.6% of patients in cycle 1 and by 6.3% in all cycles.</p> <p>Hospitalization for neutropenia occurred in 2.9% of patients during cycle 1 and in 5.6% of patients in all cycles and for febrile neutropenia in 1.7% and 3.5%, respectively.</p> <p>Grade 3/4 neutropenia occurred in 21.3% of patients in cycle 1 and in 29.5 % in all cycles; 3% and 5.7%, respectively, needed intravenous antibiotics.</p> <p>Dose reductions as reported by the investigator were needed by 7.3% of patients in cycle 2 and by 16.8% in all cycles; dose delays as reported by the investigator were needed by 7.5% and 20.1%, respectively.</p> <p>Serious adverse events were consistent with toxicities observed in patients given chemotherapy.</p> <p>In all, 15 patient deaths were attributed to infections, including 2 from septic shock. Further, 458 patients had at least one serious adverse reaction; febrile neutropenia (3%), neutropenia (3%), dehydration (3%), and nausea (2%) were the most frequently reported.</p> <p>In addition, 10 patients (0.5%) had serious adverse events that were considered related to the study drug. Bone pain (0.1%) was the only related serious adverse event reported in more than one subject.</p>
Conclusions	After being given chemotherapy, the patients in this large, community-based study treated with pegfilgrastim experienced a low rate of neutropenia, febrile neutropenia, hospitalizations related to febrile neutropenia or neutropenia, intravenous antibiotic use related to neutropenia, and chemotherapy dose reductions and delays related to neutropenia.

Impact of first and subsequent cycle pegfilgrastim on neutropenic events in patients receiving myelosuppressive chemotherapy

Discussion

Patients undergoing myelosuppressive chemotherapy seem to benefit from the use of pegfilgrastim, beginning with the first cycle of chemotherapy. These patients experienced a low incidence of neutropenic complications as well as chemotherapy dose reductions/delays resulting from neutropenia, according to the final results of the FIRST study, a large, community-based prospective trial evaluating the impact of first and subsequent cycles of pegfilgrastim on neutropenic events in patients receiving chemotherapy.

Patients enrolled in the FIRST study were at least 18 years old and diagnosed with pathologically confirmed malignancy (except for leukemia or myelodysplastic syndrome). All patients were scheduled to receive at least four cycles of chemotherapy, given every 14, 21, or 28 days. A major comorbidity as well as previous chemotherapy, radiotherapy, and biologic therapy were permitted. In particular, the team was interested in the incidence of neutropenic hospitalizations and chemotherapy dose reductions/delays; secondarily, investigators sought information on the incidence of grade 3/4 neutropenia, febrile neutropenia, intravenous antibiotic use, and adverse events.

Rates of neutropenic complications as well as dose reductions/delays favored the use of pegfilgrastim during cycle 1 (Table). Febrile neutropenia (absolute neutrophil count < 1,000/ μ L and temperature \geq 38.2°C) occurred in 3.6% of patients during cycle 1 and in 6.3% of patients in all cycles.

Cycle-1 febrile neutropenia rates reported in this community-based study were lower than published interim rates from the Awareness of Neutropenia in Chemotherapy (ANC) Registry study and were comparable to those achieved in a randomized phase III study (Vogel CL et al. *J Clin Oncol* 2005;23:1178–1184), concluded Dr. Ozer.

Rates of Neutropenic Complications With Pegfilgrastim

	CYCLE 1 % (95% CI)	ALL CYCLES ¹ % (95% CI)
Hospitalization		
For neutropenia	2.9 (2.3, 3.7)	5.6 (4.7, 6.7)
For febrile neutropenia	1.7 (1.2, 2.3)	3.5 (2.7, 4.3)
Physician-reported dose reduction		
All reasons	7.3 (6.2, 8.5) ²	16.8 (15.2, 18.5)
Due to neutropenia	1.8 (1.2, 2.4) ²	2.9 (2.2, 3.7)
Physician-reported dose delay		
All reasons	7.5 (6.4, 8.8) ²	20.1 (18.4, 21.8)
Due to neutropenia	0.9 (0.5, 1.4) ²	2.1 (1.5, 2.8)

CI = confidence interval; ¹ Maximum 8 cycles; ² In cycle 2
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Key Points

- Patients undergoing chemotherapy may benefit from pegfilgrastim use beginning in the first chemotherapy cycle.

Reference

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