

Effects of G-CSF Schedule on Leukocyte Recovery and Infection Rate in the CHOP-14 Regimen for Elderly Patients With Aggressive Lymphoma

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Origin of Study	Germany
Type of Study	RETROSPECTIVE, PARALLEL-GROUP, COHORT STUDY
Objectives	Evaluate what effect, if any, reducing the duration of granulocyte colony-stimulating factor (G-CSF, filgrastim) therapy from 10 to 7 days has on leukocyte recovery and infection rates in elderly patients with aggressive lymphomas treated with CHOP (cyclophosphamide, doxorubicin, vincristine [Oncovin], and prednisone) on an accelerated 14-day schedule (CHOP-14)
Study Design	Non-Hodgkin's lymphoma patients 61–75 years of age enrolled in the NHL-B2 trial who had received six cycles of CHOP-14 with 10 days of filgrastim support (from day 4 to day 13) in each cycle were compared with the same age group of patients in the RICOVER-60 trial who had received the identical chemotherapy as those in the NHL-B2 study but had been treated with filgrastim from day 6 to day 12 (total of 7 days) per cycle.
Patients	<p>A total of 181 patients enrolled in the NHL-B2 trial were compared with the first 63 consecutive patients enrolled in the RICOVER-60 trial who had received at least one of six planned courses of CHOP-14. In all, 306 CHOP-14 cycles documented within RICOVER-60 were analyzed.</p> <p>Both patient populations had similar International Prognostic Index risk factors, and adherence to the recommended filgrastim doses was excellent in both trials.</p>
Observations	<p>The reduced 7-day application of filgrastim in the RICOVER-60 study, compared with the full 10 days of its use in the NHL-B2 trial, resulted in a lower leukocyte nadir and a delay in leukocyte recovery by approximately 1 day but did not delay the start of the next CHOP-14 cycle.</p> <p>The rate of CHOP-14 cycles with World Health Organization (WHO) grade 3/4 infections doubled, from 2.4% in the NHL-B2 trial to 5.2% in the RICOVER-60 trial.</p> <p>The percentage of cycles in which intravenous antibiotics were used rose from 15.2% in the NHL-B2 trial to 20.8% in the RICOVER-60 trial.</p>
Conclusions	<p>Although a reduction in the number of days of concomitant filgrastim therapy does not affect the feasibility of the biweekly CHOP-14 regimen in elderly patients with aggressive lymphomas, infection rates increase considerably.</p> <p>A full 10-day application of filgrastim is therefore recommended, starting on day 4 of each cycle, in patients receiving CHOP-14.</p>
Discussion	In elderly (61–80 years old) patients with aggressive lymphoma, dose-dense CHOP chemotherapy, with standard doses administered on an accelerated 14-day schedule, is feasible with the use of colony-stimulating factors such as filgrastim (Neupogen). Compared with the classic 21-day CHOP regimen, the accelerated dosing schedule results in improved complete response rates, freedom from treatment failure, and improved overall survival rates in these patients.

G-CSF Schedule in Elderly Patients With Aggressive Lymphoma Treated With CHOP-14

In this study, Kloess and colleagues attempted to evaluate the results of a reduced application of filgrastim in elderly patients with aggressive non-Hodgkin's lymphoma. In the ongoing RICOVER-60 trial of the Deutsche Studiengruppe für Hochmaligne Non-Hodgkin Lymphome, patients are randomized to receive six or eight cycles of CHOP-14, each with and without rituximab (Rituxan). In the study group's NHL-B2 trial, filgrastim was given for 10 days (day 4 to day 13), whereas in the RICOVER-60 trial, the application of filgrastim was reduced to 7 days (day 6 to day 12). Patients in the NHL-B2 trial who had received six cycles of CHOP-14 were compared with the same age group (61–75 years) in the RICOVER-60 trial receiving the identical chemotherapy regimen.

The first 63 consecutive patients of the RICOVER-60 trial who had received at least one of six courses of CHOP-14 were compared with 181 patients of the NHL-B2 trial. Analysis was performed on 306 CHOP-14 cycles documented within the RICOVER-60 trial. Adherence to the recommended doses of filgrastim was excellent in both trials.

Although recycling at 2-week intervals was achieved with both regimens, the briefer course of filgrastim therapy resulted in a lower leukocyte nadir and delayed leukocyte recovery (by approximately 1 day). The rate of grade 3/4 infections doubled from 2.4% in the NHL-B2 trial to 5.2% in the RICOVER-60 trial; similarly, the cycles in which intravenous antibiotics were needed increased from 15.2% to 20.8%.

Based on their study findings, Kloess and colleagues recommend a 10-day application of filgrastim starting no later than day 4 of treatment in these patients. The study was supported by the Deutsche Krebshilfe and an unrestricted grant from Amgen Inc.

Key Points

- Reduced dosing of filgrastim can increase the risk of infection and use of intravenous antibiotics.
- A full 10-day dose schedule of filgrastim, which reduces the degree and depth of neutropenia, is recommended.
- An appropriate duration of treatment for filgrastim is until leukocyte recovery.

References

Kloess M, Zeynalova S, Truemper L, et al. Effects of G-CSF schedule on leukocyte recovery and infection rate in the CHOP-14 regimen for elderly patients with aggressive lymphoma. Poster presented at the 39th Annual Meeting of the American Society of Clinical Oncology; May 31–June 3, 2003; Chicago, Ill. Abstract 2402.