

Comparative Effectiveness of White Blood Cell Growth Factors on Neutropenia, Infection, and Survival in Older People with Non-Hodgkin's Lymphoma Treated with Chemotherapy

Gruschkus SK, Lairson D, Dunn JK, et al. *Journal of the American Geriatrics Society*. 2010; **58**:1885-95.

Study Overview:

Non-Hodgkin's lymphoma (NHL) is one of the most common cancer types, and incidence and mortality of NHL are rising fast. Approximately 50% of patients are 65 years or older at the time of diagnosis. In this elderly population, the myelosuppressive effect of chemotherapy, and consequently the risk of febrile neutropenia (FN), are greater than in younger patients.

Prophylactic treatment with granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF) has been shown to reduce the incidence and duration of FN and related complications in clinical trials. Current clinical guidelines recommend the use of these growth factors to support administration of the planned chemotherapy dose, to reduce FN and possibly infections. However, there is only limited evidence that CSF use positively impacts on response rate and progression-free or overall survival.

This retrospective cohort study used data from the Surveillance, Epidemiology, and End Results (SEER)-Medicare database to evaluate the efficacy of CSFs at reducing FN and infection and at improving overall survival in elderly NHL patients receiving chemotherapy in the real world setting. A total of 13,203 patients 65 years or older were included, with incident NHL diagnosed from 1992 to 2002 and who received chemotherapy within one year of diagnosis. Primary prophylaxis was defined as CSF administration before the occurrence of neutropenia, fever or infection; CSF use after any of these events was considered secondary prophylaxis. FN was defined as the documentation of both neutropenia and fever. Only infections occurring within 28 days of chemotherapy were included.

Key Findings:

- Overall, 1,339 patients (10%) received CSF primary prophylaxis; 3,927 patients (30%) received secondary prophylaxis, and 7,937 patients (60%) received no CSF.
- Of those patients with primary prophylaxis, 90% received G-CSF only, 4% received GM-CSF only, and 6% received both; these proportions were similar in patients with secondary prophylaxis (86%, 7% and 7%).
- Multivariate logistic regression analysis demonstrated that, after adjusting for relevant demographic, clinical and treatment characteristics, patients with 5-9 CSF administrations as primary prophylaxis had a 42% lower risk of FN (odds ratio [OR] 0.58; 95% confidence interval [CI] 0.41 to 0.83) compared to patients without CSF. In patients receiving ≥ 10 CSF administrations as primary prophylaxis, the risk of FN was reduced by 48% (OR 0.52; 95% CI 0.36-0.76).

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- The protective effect of primary CSF prophylaxis was strongest in patients who received the highest number of chemotherapy doses \leq 5 doses: OR 0.80; 95% CI 0.52-1.18; 11-25 doses: OR 0.38; 95% CI 0.28-0.50; > 25 doses: OR 0.43; 95% CI 0.31-0.62).
- Primary CSF prophylaxis appeared to have a more pronounced protective effect in patients with diffuse large B-cell lymphoma than in patients with follicular lymphoma or those with other histologies.
- The incidence of infection was reduced by 27% in patients with 5-9 administrations (OR 0.73; 95% CI 0.55 to 0.96) and by 52% in those receiving \geq 10 administrations (OR 0.48; 95% CI 0.35 to 0.66).
- Cox proportional hazards analysis showed that primary CSF prophylaxis was not associated with increased overall survival.
- In the subset of patients who experienced neutropenia, fever or infection (n = 8,546), after adjustment for relevant covariates, the risk of mortality was reduced by 9% in patients receiving 4-10 administrations of secondary CSF prophylaxis (hazard ratio [HR] 0.91; 95% CI 0.84 to 0.99), by 23% in patients receiving 11-23 administrations of secondary CSF prophylaxis (hazard ratio [HR] 0.77; 95% CI 0.71 to 0.84) and by 13% in patients receiving > 23 administrations of secondary CSF prophylaxis (hazard ratio [HR] 0.87; 95% CI 0.79 to 0.95) compared with patients without secondary CSF prophylaxis.

Conclusions:

This study was the first large population-based cohort study to evaluate clinical outcomes of CSF use in elderly NHL patients receiving chemotherapy. Results suggest that primary CSF prophylaxis effectively prevented FN and infection, although it did not significantly improve overall survival. Administration of CSF as secondary prophylaxis was associated with significantly longer overall survival in patients experiencing neutropenic complications. The authors conclude that these findings substantiate clinical guidelines recommending prophylactic CSF in elderly NHL patients receiving chemotherapy, regardless of neutropenia risk threshold, and provide important information to geriatricians. Given the continued uncertainty regarding an effect of CSF use on long-term outcomes, future research should further evaluate its utility.

<http://www.ncbi.nlm.nih.gov/pubmed/20840455>