

## Risk of Mortality in Patients with Cancer Who Experience Febrile Neutropenia

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### Study Overview:

In cancer patients undergoing myelosuppressive chemotherapy, the risk of developing potentially life-threatening febrile neutropenia (FN) is determined by patient-, disease- and treatment-related factors. Primary prophylaxis with granulocyte colony-stimulating factor (G-CSF) has been shown to reduce FN risk.

FN has been reported to be associated with significant morbidity and early mortality and may also impact on the treatment plan by causing dose reductions or delays, chemotherapy discontinuation, or a switch to potentially less effective regimens.

This retrospective cohort study investigated the impact of FN on mortality and hospitalisation in a large US managed health plan database linked to the National Death Index. A total of 11,980 patients with Non-Hodgkin lymphoma (NHL), breast, ovarian, lung or colorectal cancer and a first chemotherapy claim between 2001 and 2006 were included in the analysis. FN was classified as a primary or secondary diagnosis of neutropenia or infection during the first course of chemotherapy. Within one tumour type, patients with and without FN were matched by propensity score to maximise comparability.

The primary outcome was overall mortality; secondary outcomes were early mortality, defined as all-cause mortality during the first course of chemotherapy, and all-cause hospitalisation during the first course of chemotherapy.

### Key Findings:

- The incidence of both overall and early mortality, as well as that of hospitalisations, was highest for lung cancer and lowest for breast cancer.
- Across all cancer types, there was a non-significant trend towards a higher incidence of overall mortality in patients with vs without FN (6.12 per 1000 person-months [PM]; 95% confidence interval [CI] 5.66 to 6.61/1000 PM; vs 5.48/1000 PM; 95% CI 5.05 to 5.94/1000 PM).
- NHL was the only cancer type for which overall mortality was significantly higher in patients with vs without FN (8.22/1000 PM; 95% CI 6.21 to 10.87/1000 PM; vs 4.29/1000 PM; 95% CI 2.96 to 6.21/1000 PM).
- The incidence of early mortality was significantly higher in patients with FN vs those without FN (8.59/1000 PM; CI 7.61 to 9.71/1000 PM; vs 5.56/1000 PM; 95% CI 4.70 to 6.57/1000 PM).
- The incidence of hospitalisation was significantly greater for patients with vs without FN (44.41/1000 PM; CI 42.47 to 46.44/1000 PM; vs 21.45/1000 PM; 95% CI 20.17 to 22.81/1000 PM).

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- Significantly more patients with FN received G-CSF primary prophylaxis as compared with patients without FN (34.97% vs 21.04%;  $p < 0.001$ ).
- Cox multivariate regression analysis controlled for a wide range of covariates and showed that FN significantly increased the risk of overall mortality (hazard ratio [HR] 1.15; 95% CI 1.02 to 1.29;  $p = 0.02$ ), early mortality (HR 1.35; 95% CI 1.09 to 1.67;  $p = 0.006$ ) and hospitalisation (HR 2.04; 95% CI 1.89 to 2.20;  $p < 0.001$ ).
- In these Cox multivariate regression models, G-CSF primary prophylaxis was associated with a 35% decrease in overall mortality (HR 0.65; 95% CI 0.53 to 0.79;  $p < 0.001$ ) and a 45% decrease in early mortality (HR 0.55; 95% CI 0.40 to 0.76;  $p < 0.001$ ).

### Conclusions:

This retrospective cohort study of data from a real-life clinical practice setting demonstrated a significant increase in the risk of overall and early mortality, and of hospitalisation, in cancer patients who experienced FN during chemotherapy compared with those who did not. In this study, the primary impact of FN appeared to be on early mortality; extended evaluation of the association between overall mortality and FN was limited due to a median follow-up of 17.6 months. Prophylactic G-CSF was received by 14% more patients with FN, which probably reflects targeting of prophylaxis to patients who had an inherently greater risk of FN. The authors state that the results were consistent with findings from other clinical and investigational trials indicating that FN had a significant impact on cancer patient mortality.

<http://www.ncbi.nlm.nih.gov/pubmed/20715160>