

Febrile neutropenia and related complications in breast cancer patients receiving pegfilgrastim primary prophylaxis versus current practice neutropaemia management: Results from an integrated analysis

von Minckwitz G, Schwenkglenks M, Skacel T, et al. *Eur J Cancer*. 2009;**45(4)**:608-17.

Study overview: Febrile neutropenia (FN) is a consequence of myelosuppressive chemotherapy and can be life-threatening, with a mortality rate of up to 10%. Moreover, FN events can cause dose delays and/or reductions, which negatively impact on survival in breast cancer patients receiving adjuvant treatment. Granulocyte colony-stimulating factor (G-CSF) prophylaxis is effective at decreasing the incidence of FN; however, G-CSF use in current practice appears to be inconsistent.

This integrated analysis included individual patient data from 11 clinical trials and observational studies on breast cancer using chemotherapy regimens with an FN risk $\geq 15\%$. FN rates and FN-related outcome measures were compared in patients receiving two different types of neutropenia prophylaxis: primary prophylaxis with pegfilgrastim (PPP, $n = 1303$), defined as the use of pegfilgrastim from the first chemotherapy cycle, or current practice neutropenia management (CP, $n = 979$), defined as any current approach (no G-CSF or daily G-CSF/pegfilgrastim in any cycle).

Key findings:

- **In the CP group, 75% of patients did not receive G-CSF in cycle 1**, and despite 10% of patients experiencing cycle 1 FN, this proportion remained similar in cycles 2 and 4. **Typically, 5 -7 doses of daily G-CSF were administered per cycle**; in cycle 1, 49% of patients receiving daily G-CSF had less than 7 doses.
- A generalised linear mixed model identified **CP vs. PPP, older age, and stage IV vs. stage I-III disease as predictors of FN** across all cycles and in cycle 1. FN rates were lower in the PPP group, both in a descriptive analysis (5% vs. 16%) and after baseline adjustment for age, study, and disease stage (5% vs. 29%). When age and disease stage were included in the model, the odds of FN occurrence was significantly lower with PPP (FN across all cycles: odds ratio [OR] 0.12 [0.08, 0.19]; $p < 0.0001$; cycle 1 FN: OR 0.11 [0.06, 0.20]; $p < 0.0001$).
- The **incidence of FN-related hospitalisation and dose reductions $\geq 15\%$, but not dose delays ≥ 3 days, were influenced by the type of prophylaxis, age, and disease stage**. Mixed model analysis demonstrated significantly lower odds of FN-related hospitalisation (OR 0.21 [0.12, 0.34]; $p < 0.0001$) and dose reductions (OR 0.58 [0.41, 0.83]; $p = 0.0027$) in the PPP group.
- **Grade 3-4 haematological toxicity was predicted by the type of neutropenia prophylaxis and age**, but not by disease stage. The odds of grade 3-4 neutropenia and leucopenia were significantly lower with PPP as compared to CP (neutropenia: OR 0.04 [0.03, 0.06]; $p < 0.0001$; leucopenia: OR 0.06 [0.04, 0.08]; $p < 0.0001$).

You can contact the INC-EU co-ordinating centre at: info@inceu.org
Telephone: +41 (0) 41 377 48 39 Fax: +41 (0) 41 377 48 35

Conclusions: This integrated analysis confirms increasing age and advanced disease as important patient-related risk factors for FN. Mixed model analysis shows that PPP, as compared to CP, reduces the odds of FN and FN-related complications in breast cancer patients receiving myelotoxic chemotherapy. These results support the use of PPP in patients receiving chemotherapy with a moderately-high to high FN risk, both to avoid FN and to enable delivery of planned chemotherapy.

<http://www.ncbi.nlm.nih.gov/pubmed/19110415>

You can contact the INC-EU co-ordinating centre at: info@inceu.org
Telephone: +41 (0) 41 377 48 39 Fax: +41 (0) 41 377 48 35