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Evidence Assessment: Summary of a Systematic Review

Who is this summary for?
Policy makers or clinicians who have to make decisions about the treatment and care of patients with breast cancer.

Primary prophylactic colony-stimulating factors for the prevention of chemotherapy-induced febrile neutropenia in breast cancer patients

Key findings

- Prophylactic treatment with colony-stimulating factors significantly reduces the risk of developing febrile neutropenia by 73%.
- The estimated number of patients needed to be treated with colony-stimulating factors in order to prevent one event of febrile neutropenia is 12.
- Although a significant decrease in all-cause mortality was noted, there was no reduction in infection-related mortality in patients on chemotherapy who received colony-stimulating factor therapy.

Background

Patients with breast cancer receiving chemotherapy have an increased risk of infection mediated through a low number of protective white blood cells (neutropenia). Neutropenia is a common toxicity of many chemotherapy agents and is caused by the suppression of the bone marrow. The first sign of infection is usually a fever, which indicates a potentially life threatening condition if it occurs during severe neutropenia (febrile neutropenia). Febrile neutropenia requires hospital care including the administration of intravenous antibiotics and possible delays in the continuation of chemotherapy. Colony-stimulating factors are drugs administered during chemotherapy in order to prevent or reduce the incidence or duration of febrile neutropenia and neutropenia.

Question

What is the efficacy and safety of primary prophylactic colony-stimulating factors compared to placebo or no treatment for the prevention of febrile neutropenia in patients with breast cancer undergoing chemotherapy?

Primary prophylactic for the prevention of chemotherapy in breast cancer patients in Cameroon: Data on cancers are rare in Cameroon because of the unavailability of cancer registries. However, some studies demonstrate that breast cancers account for about 11% of all malignancies diagnosed in Cameroon. Interventions such as surgery, radiotherapy, hormonal therapy, occasionally chemotherapy or a combination of these methods are the most common observed. The use of primary prophylactic colony-stimulating factors could prevent the occurrence of febrile neutropenia in patients with breast cancer undergoing chemotherapy.

Table 1: Summary of the systematic review		
	What the review authors searched for	**What the review authors found**
Studies	Randomized controlled trials (RCT)	Eight RCTs met the inclusion criteria.
Participants	Patients with breast cancer at any stage of disease undergoing treatment with any type and dosage of chemotherapy who were at risk of experiencing febrile neutropenia or neutropenia.	Trials included patients ranged from 18 to 78 years and the mean age was approximately 50 years.
Interventions	The intervention group received any kind of either granulocyte colony-stimulating factors or granulocyte-macrophage - colony-stimulating factors at any administered dosage as primary prophylaxis during each cycle of standard non-myeloablative chemotherapy prior to the onset of neutropenia in the treatment of breast cancer.	Six trials used granulocyte colony-stimulating factors: one trial compared lenograstim with placebo, two trials compared pegfilgrastim with placebo, two trials used filgrastim compared with no treatment and one trial used a biosimilar filgrastim compared with filgrastim and with no treatment.
Controls	1. Identical chemotherapy regimen as the intervention group and a placebo 2. No treatment	Placebo.
Outcomes	**Primary outcomes** 1. Proportion of patients with febrile neutropenia. 2. Duration of febrile neutropenia. 3. Early mortality. 4. Infection-related mortality. **Secondary outcomes** • Proportion of patients with neutropenia • Duration of neutropenia • Proportion of patients being hospitalized or treated, or both, with antibiotics because of febrile neutropenia • Duration of hospitalization and antibiotic treatment. • Administration of chemotherapy (e.g. number of dose delays or dose reductions, relative dose intensity) • Incidence of colony-stimulating factors - related adverse effects (e.g. bone pain and injection-site reaction)	Two trials described the number of patients with febrile neutropenia as the primary outcome. The six remaining trials reported different primary outcomes: duration of grade IV neutropenia, number of neutropenic events, disease-free survival and duration of severe neutropenia.
Date of the most recent search: 8 August 2011.		
Limitations: This is a moderate quality systematic review with limitations related to the included studies, AMSTAR =9/11.		
Citation: Renner P, Milazzo S, Liu JP, Zwahlen M, Birkmann J, Horneber M. Primary prophylactic colony-stimulating factors for the prevention of chemotherapy-induced febrile neutropenia in breast cancer patients. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD007913. DOI: 10.1002/14651858.CD007913.pub2		

Table 2: Summary of findings

Outcomes	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Febrile neutropenia	0.27 [0.1-0.70]	2073 (6)	**Moderate**	The eight included RCTs differed with regards to their risk of bias and

Early mortality	0.32 [0.13-0.77]	2143 (8)	**Low**	quality of reporting. Only two trials were judged as having only minor deficiencies in methodological quality.
Infection-related mortality	0.14 [0.02-1.29]	2143 (8)	**Low**	

Applicability

In this review two trials were conducted in France and one in each of the following countries: USA, Denmark, Italy, Brazil and Finland. Even though none of these studies was conducted in Africa, some of these interventions can be applied in low resource settings.

Conclusions

The evidence that the administration of colony-stimulating factors could reduce early all-cause mortality is weak. There was no reduction in risk of infection-related mortality with colony-stimulating factors treatment.

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March 2014