

# Phase III Trial Comparing Granulocyte Colony-Stimulating Factor to Leridistim in the Prevention of Neutropenic Complications in Breast Cancer Patients Treated with Docetaxel/Doxorubicin/Cyclophosphamide: Results of the BCIRG 004 Trial

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## Abstract

This randomized, double-blind, phase III trial compared granulocyte colony-stimulating factor (G-CSF; filgrastim) and leridistim (formerly myelopoietin), a chimeric dual agonist that binds both G-CSF and interleukin-3 receptors, for the prevention of neutropenic complications in patients with breast cancer receiving TAC (docetaxel/doxorubicin/cyclophosphamide) chemotherapy. Patients with metastatic (44%) or localized breast cancer (56%) were randomized to G-CSF 5 µg/kg subcutaneously (s.c.) daily (n = 135), leridistim 5 µg/kg s.c. daily (n = 139), or leridistim 10 µg/kg s.c. every other day alternating with placebo (n = 139). Following administration of TAC (docetaxel 75 mg/m<sup>2</sup>, doxorubicin 50 mg/m<sup>2</sup>, cyclophosphamide 500 mg/m<sup>2</sup>) on day 1, patients received growth factor beginning on day 2 until the postnadir absolute neutrophil count exceeded 1500 cells/µL. Chemotherapy cycles were repeated every 21 days. The incidence of febrile neutropenia was 7% in the G-CSF arm, 19% in the daily leridistim arm ( $P = 0.003$  for comparison with G-CSF) and 22% in the alternate-day leridistim arm ( $P < 0.001$  for comparison with G-CSF). There was no significant difference between treatment arms in the cumulative percentage of patients experiencing grade 4 neutropenia at some point during therapy (85%-88%). However, grade 4 neutropenia occurred in 53% of cycles in the G-CSF cohort, 61% of cycles in the daily leridistim group ( $P = 0.063$  for comparison with G-CSF), and 63% of cycles in the alternate-day leridistim group ( $P = 0.015$  for comparison with G-CSF). We conclude that G-CSF is superior to leridistim in the prevention of febrile neutropenia in patients with advanced breast cancer receiving TAC chemotherapy. The up-front prophylactic use of G-CSF is a reasonable supportive therapy for patients treated with docetaxel/anthracycline-based combination chemotherapy.

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## Introduction

In women with metastatic breast cancer, the use of combination chemotherapy generally yields greater response rates than monotherapy. Likewise, in the adjuvant setting, the use of polychemotherapy improves outcomes compared with administration of single agents.<sup>1</sup> The use of combination regimens has therefore become standard for the treatment of women with breast cancer.

Numerous cytotoxic compounds have been incorporated into combination regimens, including cyclophosphamide, doxorubicin, epirubicin, fluorouracil, methotrexate, and mitomycin.<sup>2</sup> Recently, taxanes such as paclitaxel and docetaxel