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/m², doxorubicin 50 mg/m², cyclophosphamide 500 mg/m²) 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 any 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.


Key words: Myelopoietin, Febrile neutropenia, Filgrastim, Prophylaxis, Interleukin-3 receptor