

ELYPSE 2: a prospective randomized trial comparing filgrastim in primary and secondary prophylaxis in patients at high risk for febrile neutropenia

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Origin of Study	France
Type of Study	PROSPECTIVE, RANDOMIZED, PHASE II TRIAL
Objectives	Compare filgrastim (Neupogen) in primary versus secondary prophylaxis in a high-risk group of patients with solid tumors or non-Hodgkin's lymphoma (NHL).
Study Design	<p>The observed incidence of febrile neutropenia was 40% for patients having lymphocyte counts $\leq 700/\mu\text{L}$ on day 1 and 66% for those having such measurements on day 5.</p> <p>In one arm, patients received 300–480 $\mu\text{g}/\text{d}$ of filgrastim from days 6–12 as primary prophylaxis; in the other, patients received the same doses of the drug as secondary prophylaxis following febrile neutropenia.</p> <p>The primary endpoint was the rate of grade 4 febrile neutropenia. The team hypothesized that a 40% drop in the risk of febrile neutropenia would result from primary prophylaxis.</p>
Patients	<p>Patients were ≥ 18 years of age (median age, 53 years; 54% male) and were diagnosed with solid tumors or NHL; patients had day 1 or 5 lymphocyte counts $\leq 700/\mu\text{L}$, underwent high-risk chemotherapy, and were judged to be at high risk of febrile neutropenia after chemotherapy.</p> <p>The most frequent tumors found were sarcomas (36%), breast cancers (18%), lymphomas (15%), head and neck cancers (10%), and lung cancers (6%).</p> <p>In all, 137 patients in 7 centers were included. Further, 23% of patients had a performance status > 1 when given the first line of chemotherapy.</p>
Observations	<p>No difference in the duration of hospitalization or antibiotic therapy was seen between the groups.</p> <p>The median number of days of filgrastim use was 14 (range, 0–24 days) for the primary prophylaxis arm vs 0 days (range, 0–17 days) for the secondary prophylaxis group.</p> <p>After the first course, grade 4 febrile neutropenia occurred in 38% of patients in the secondary prophylaxis group and 25% of the primary prophylaxis group, showing a 34% reduction of febrile neutropenia in the primary prophylaxis arm. Further, primary prophylaxis was associated with a significant reduction of febrile neutropenia using logistic regression ($P = 0.04$).</p> <p>In all, 22% of patients in the secondary prophylaxis group suffered febrile neutropenia after the second course.</p> <p>Among a subgroup of patients having a performance status > 2 and lymphocyte counts $\leq 700/\mu\text{L}$ (signifying a reported 20% risk of early death), 2 of 8 patients (25%) died after the first course, whereas none of the 13 in the filgrastim group died. This difference was not significant in the whole group.</p>
Conclusions	<p>Lymphopenic patients receiving high-risk chemotherapy are at high risk of febrile neutropenia.</p> <p>Primary prophylaxis with filgrastim reduces the incidence of febrile neutropenia.</p>

Filgrastim as primary and secondary prophylaxis in patients at high risk for febrile neutropenia

Discussion

Cytotoxic chemotherapy is a life-threatening consequence of febrile neutropenia. Use of granulocyte colony-stimulating factor reduces the risk of febrile neutropenia; however, this treatment may be cost-efficient only if the incidence of febrile neutropenia is at least 20%. Dr. Biron discussed the results of a randomized phase II trial of filgrastim given as primary and secondary febrile neutropenia prophylaxis in a high-risk group of lymphopenic patients.

The investigative team sought a 25% reduction in febrile neutropenia using primary prophylaxis. A total of 137 patients with a lymphocyte count of $\leq 700/\mu\text{L}$ following high-risk chemotherapy were randomized to receive primary (filgrastim given from days 6–12 during the first chemotherapy course) or secondary prophylaxis (no filgrastim given during the first course; if febrile neutropenia occurred after the first course, filgrastim was given from days 6–12 of the second chemotherapy course).

According to Dr. Biron, after the first course of chemotherapy, grade 4 febrile neutropenia occurred in 25% of those given primary prophylaxis and 38% of those given secondary prophylaxis, showing a 34% reduction among those given primary prophylaxis ($P = 0.14$). In addition, 22% of patients given secondary prophylaxis experienced febrile neutropenia after the second course. A median of 6 days of hospitalization was needed during the first course by patients given primary prophylaxis and 7 days for those given secondary prophylaxis; a median of 14 days and 13 days of hospitalization, respectively, was needed during the entire duration of treatment.

Key Points

- Primary filgrastim prophylaxis may be cost-efficient in managing patients treated with cytotoxic chemotherapy.

Reference

Biron P, Ray-Coquard I, Le Cesne A, et al. ELYPSE 2: a prospective randomized trial comparing filgrastim in primary and secondary prophylaxis in patients at high risk for febrile neutropenia. Presented at the 42nd Annual Meeting of the American Society of Clinical Oncology; June 2–6, 2006; Atlanta, Georgia. Abstract 8614.