INTRODUCTION

As a standard of practice, G-CSF products require administration 24 hours after chemotherapy.

Eflapegrastim (ROLONTIS®) is a long-acting granulocyte-colony stimulating factor (G-CSF), consisting of a recombinant human G-CSF analog conjugated to a human IgG1 Fc fragment via a short polypeptide glycosyl linker. Eflapegrastim is not a biobarrier and represents the first long-acting myeloid growth factor that is the subject of a pending innovator biologic license application in more than 18 years.

In two Phase 3 studies that randomized a total of 645 patients with early-stage breast cancer (ESBC) to either eflapegrastim (3.6 mg G-CSF in 0.6 mL) or pegfilgrastim (8 mg G-CSF in 0.6 mL) given 24 hours after doxorubicin and cyclophosphamide (AC) administration, the duration of severe neutropenia (DSN) was statistically noninferior in patients treated with eflapegrastim compared to pegfilgrastim, despite eflapegrastim being given at 80% of the G-CSF dose of pegfilgrastim.

In preclinical studies with chemotherapy-induced neutropenic rats compared to pegfilgrastim (Neulasta®), the duration of severe neutropenia (DSN) was statistically noninferior in patients treated with eflapegrastim compared to pegfilgrastim to provide effective prophylaxis against chemotherapy-induced neutropenia when administered on the same day as chemotherapy.

OBJECTIVES

To assess the feasibility of eflapegrastim dosing on the same-day as docetaxel/cyclophosphamide (TC) in patients receiving TC for treatment of ESBC.

To dose schedule finding assessment of eflapegrastim administration at either 0.5 hours, 3 hours, or 5 hours from the end of TC administration.

STUDY DESIGN

- **Phase 1, open-label, multi-center trial**
  - Intravenous (IV) administration of TC on Day 1 of each cycle will be as follows:
    - Docetaxel 75 mg/m² in 90 minutes.
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          - Docetaxel 75 mg/m² in 90 minutes.

- **Endpoints**
  - **Primary:** Duration of Grade 4 neutropenia (ANC < 0.5 x 10⁹/L) in Cycle 1
  - **Secondary:**
    - Incidence of Grade 4 neutropenia (ANC < 0.5 x 10⁹/L) in Cycle 1
    - Time to recovery to ANC ≥1.5 x 10⁹/L in Cycle 1
    - Incidence of Grade 5 neutropenia in Cycle 1 (WCC ≤ 0.5 x 10⁹/L) and either a single temperature of ≥38°C (≥100.4°F) for more than 1 hour, or a sustained temperature of ≥38°C (≥100.4°F) for a 24-hour period.
    - Pharmacokinetics (PK) of eflapegrastim in Cycle 1
    - Incidence of neutropenic complications during Cycle 1

- **Safety:**
  - Periperal blood count (ANC ≤ 0.5 x 10⁹/L)
  - Skin reactions (≥30% body surface area)
  - Clinical laboratory abnormalities

**Safety**

Patients may receive premedications for chemotherapy prophylaxis and on Cycle 2, Day 1 (Day 22) before TC dose.

Blood for CBC and PK analysis will be drawn before TC dose on Day 1 and 13.2 mg/0.6 mL (3.6 mg G-CSF) fixed dose eflapegrastim administered subcutaneously (SC) at 0.5, 3, or 5 hours after TC.

Blood for CBC and PK analysis will be drawn before TC dose on Cycle 1, Days 9 and 10 (±1 day), and on Cycle 2, Days 1 and 2 before TC dose.

Peripheral blood counts will be drawn daily from Day 2 to Day 10.

**Key Inclusion Criteria**

- Histologically confirmed (operable stage I-III) patients with ESBC
- Patients 18 years and older
- WHO performance status (Karnofsky) ≥ 70%
- Adequate hematological, renal, and hepatic function
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**Key Exclusion Criteria**

- Recurrent/metastatic breast cancer
- Active concurrent malignancy
- Known sensitivity or previous reaction to E. coli-derived products, or any products to be administered during study
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**Participants**

- Target accrual: 45 patients randomized 1:1:1 to 30 min, 3 hr and 5 hr dosing
- A sample size of 15 patients per dosing schedule arm was determined to provide adequate precision for the 95% CI of the DSN and secondary endpoints, including PK parameters.

**Sample size**

- The sample size produces a 2-sided 95% CI with a distance from the mean DSN of the limits that is equal to ±0.55 using t-distribution when the estimated standard deviation is 1.0 days.
- A safety evaluation will be performed once the first three patients in each arm have completed Cycle 1.

**Current Enrollment**

- Enrollment began in April 2020
- 9 of 45 patients have been enrolled to date.