Interim safety evaluation of same-day dosing of eflapegrastim* in patients with early-stage breast cancer (ESBC) receiving docetaxel and cyclophosphamide (TC)

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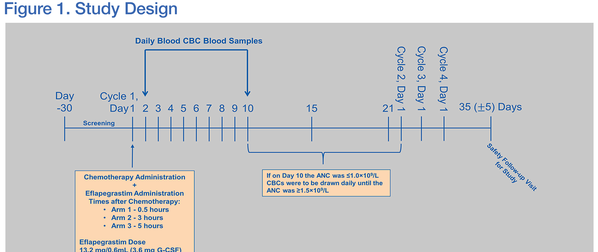
BACKGROUND

Eflapegrastim

- Patients receiving chemotherapy are at risk of developing neutropenia (CIN) that can lead to FN and/or infection, necessitating dose delays and dose reductions, which can affect clinical outcomes.[1,2]
- Clinical Practice Guidelines recommend the use of G-CSF as primary prophylaxis when the anticipated risk of FN is high.
- G-CSF including long-acting agents, is administered 24 hours after chemotherapy, which requires patients to return to the clinic the next day.
- Eflapegrastim (ROLONTIS®) is a novel long-acting G-CSF, produced by covalent conjugation of a human G-CSF analog and IgG4 Fc fragment, linked via a short polyethylene glycol linker.[3,4]
- The increased FcRn-mediated transcytosis of eflapegrastim observed in preclinical studies may enhance its bioavailability post-chemotherapy allowing dosing on the same day as chemotherapy.[5]

METHODS

Figure 1. Study Design



Key Inclusion Criteria

- Patients with histologically confirmed stage I-IIIA early-stage breast cancer (ESBC)
  - ECOG Performance Score <=2
  - Candidates for neoadjuvant or adjuvant cyclophosphamide and docetaxel (TC)
- Age ≥ 18 years

Key Exclusion Criteria

- Prior exposure or known sensitivity to G-CSF
- History of bone marrow or hematopoietic stem cell transplant
- Radiotherapy, surgery or treatment with investigational agent within 30 days prior to enrollment

Study Endpoints

- Primary Endpoint:
  - Duration of Grade 4 neutropenia (ANC <0.5×10⁹/L) in Cycle 1
- Secondary Endpoints:
  - Incidence of Grade 3 febrile neutropenia (FN) in Cycle 1
  - Safety

INTERIM SAFETY EVALUATION

Per protocol

Safety evaluation proceeded following completion of Cycle 1 for the first 3 patients in all treatment arms. Treatment arm(s) were to be stopped for further enrollment if one of the following criteria were met:

- *2 of 3 patients reported Grade 4 neutropenia and DSN > 1 day*
- *2 of 3 patients reported febrile neutropenia in Cycle 1 and/or occurrence of any eflapegrastim-related Grade 4 AE*

Additional Safety Considerations

- Incidence of Grade 3/4 AEs in Cycle 1

DEMOGRAPHICS

- Three patients each were randomized to Arm 1, Arm 2, or Arm 3.
- All patients were evaluable for safety

Table 1. Demographics

Characteristic	Arm 1 (0.5 hrs) (N=3)	Arm 2 (3 hrs) (N=3)	Arm 3 (5 hrs) (N=3)
Age (years), Mean	48.7	63.7	59.3
Weight (kg), Mean	73.5	115.5	70.5
Gender (F/M), n/n	3/0	3/0	2/1
ECOG Performance Status, n			
0	2	1	2
1	1	2	1

RESULTS

Table 2. Severe Neutropenia in Cycle 1

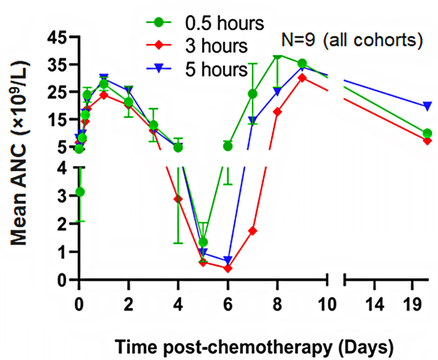
Duration of Severe Neutropenia (Days)	Arm 1 (0.5 hrs) (N=3)	Arm 2 (3 hrs) (N=3)	Arm 3 (5 hrs) (N=3)
Duration of Severe Neutropenia*			
0 days, n	2	2	1
1 days, n	1	0	1
2 days, n	0	1	1
Patients with Febrile Neutropenia, n			
Grade 3	0	0	1
Grade 4	0	1	0

* Grade 4

Note: All 9 patients received Cycle 2 chemotherapy

- **Arm 1:** ANC recovery is more rapid as compared to Arms 2 and 3
- **Arms 2 and 3:** ANC nadir is deeper and longer as compared to Arm 1

Figure 2. ANC Profiles in each Treatment Arm



OVERALL SAFETY

Table 3. Adverse Events Overview

	Arm 1 (0.5 hrs) (N=3)	Arm 2 (3 hrs) (N=3)	Arm 3 (5 hrs) (N=3)
Patients with Treatment-Emergent AEs, n			
All Grades	3	3	3
Grade 3	2	3	3
Grade 4	1	2	2
Serious AEs	0	3*	0

* Serious AEs:

1 patient – cholecystitis acute, nephrolithiasis, Urinary tract infection bacterial; 1 patient – sepsis; and 1 patient – hypertensive crisis

CONCLUSIONS

- **Arm 1**
  - Positive early data showing ANC rapid recovery in Arm 1
  - Met the prespecified interim safety evaluation criteria and therefore supports the expansion of this arm to 15 patients
  - The overall safety profile was similar to previously seen in large randomized studies when GCSF was given 24hrs after chemotherapy[3,4]
- **Arms 2 and 3**
  - ANC nadir appears deeper and longer than in Arm 1
  - Arm 2-3 did not meet the prespecified criteria, leading to stopping enrollment

Overall

- Early results are promising but a larger number of patients need to be studied before feasibility in humans is established

REFERENCES

1. Dale DC, et al. A systematic literature review of the efficacy, effectiveness, and safety of filgrastim. Support Care Cancer 2018; 26: 7-20.
2. Denduluri N, et al. Dose Delays, Dose Reductions, and Relative Dose Intensity in Patients With Cancer Who Received Adjuvant or Neoadjuvant Chemotherapy in Community Oncology Practices. J Natl Compr Canc Netw 2015; 13: 1383-93.
3. Schwartzberg LS, et al. Eflapegrastim, a Long-Acting Granulocyte-Colony Stimulating Factor for the Management of Chemotherapy-Induced Neutropenia: Results of a Phase III Trial. The Oncologist. 2020;25:1-9.
4. Cobb PW, et al. A comparison of eflapegrastim to pegfilgrastim in the management of chemotherapy-induced neutropenia in patients with early-stage breast cancer undergoing cytotoxic chemotherapy (RECOVER): A Phase 3 study. Cancer Med 2020; 9: 6234-6243.
5. Barrett JA, et al. Eflapegrastim's enhancement of efficacy compared with pegfilgrastim in neutropenic rats supports potential for same-day dosing. Exp Hematol 2020; 92: 51-61.

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***Eflapegrastim is an investigational drug not approved by the FDA**