Efbemalenograstim alfa significantly reduces incidence of incidence of severe chemotherapy-induced neutropenia in later cycles: Results of a meta-analysis

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INTRODUCTION

- Chemotherapy-inducted neutropenia (CIN) is a common and a serious hematological toxicity associated with myelosuppressive chemotherapy, often requiring dose reductions or delays in chemotherapy.
- Efbemalenograstim alfa, a novel, non-PEGylated, long-acting, human granulocyte-colony stimulating factor (G-CSF) was evaluated for the management of CIN.[1]
  - Efbemalenograstim alfa contains two human G-CSFs fused with human IgG2-FC via a short peptide linker, a structure that allows once-per-cycle administration for the reduction of CIN.
  - Non-PEGylation of efbemalenograstim alfa may eliminate PEGylation effects on immunogenicity and reduced efficacy of pegfilgrastim during later chemotherapy cycles.
- Efbemalenograstim alfa, a non-PEGylated, long-acting, human granulocyte-colony stimulating factor was recently evaluated for the management of chemotherapy-induced neutropenia in a phase III trial of 393 patients with stage I-III invasive breast cancer.[2]
- The study met the primary end point, demonstrating that a single dose of efbemalenograstim alfa was noninferior to pegfilgrastim, decreasing the duration of severe neutropenia in cycle 1. An additional endpoint of the phase III trial was the incidence of severe neutropenia (ISN; grade 4, ANC $<0.5 \times 10^9$/L) across all chemotherapy cycles.

OBJECTIVE

- The primary objective of the current study was to conduct a meta-analysis of the incidence of severe neutropenia (ISN; grade 4, ANC $<0.5 \times 10^9$/L) across all chemotherapy cycles in previous trials of efbemalenograstim alfa and different chemotherapy regimens in patients with stage I-III invasive breast cancer.

METHODS

- ISN rates from four cycles from phase III trials of efbemalenograstim alfa and three different chemotherapy regimens were evaluated and compared to pegfilgrastim and filgrastim.
- **Trial 1:** Efbemalenograstim alfa + docetaxel + cyclophosphamide (TC)[2]
- **Trial 2:** Efbemalenograstim alfa + epirubicin + cyclophosphamide (EC)[3]
- **Trial 3:** Efbemalenograstim alfa + high myelotoxic docetaxel + doxorubicin (TA)[4]
  - Historic pegfilgrastim and filgrastim comparative data were evaluated.[5,6]

RESULTS

BASELINE CHARACTERISTICS & DEMOGRAPHICS

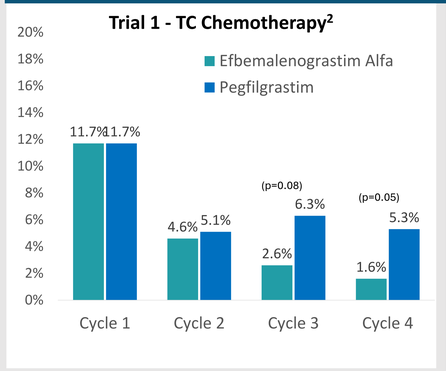
Trial 1[2] TC Chemotherapy	Efbemalenograstim Alfa (n = 197)	Pegfilgrastim (n = 196)
Age, mean years (SD)	51.4 (11.82)	53.4 (11.11)
Baseline ECOG PS		
0	153 (77.7%)	146 (74.5%)
1	44 (22.3%)	50 (25.5%)
2	--	--
Cancer Stage at Screening		
I	30 (15.2%)	34 (17.3%)
II	99 (50.3%)	107 (54.6%)
III	68 (34.5%)	55 (28.1%)
IV	--	--
Days from Diagnosis, mean (SD)	67.8 (131.98)	69.2 (260.34)

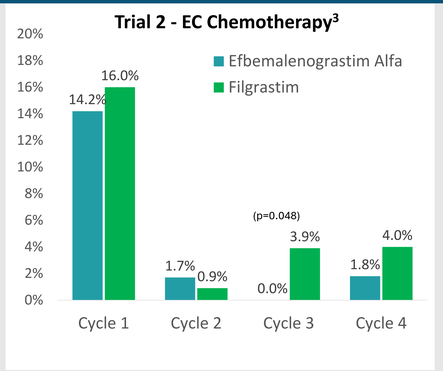
Trial 2[3] EC Chemotherapy	Efbemalenograstim Alfa (n = 122)	Filgrastim (n = 120)
Age, mean years (SD)	49.1 (9.32)	48.5 (9.14)
Baseline ECOG PS		
0	26 (21.7%)	35 (29.4%)
1	94 (78.3%)	83 (69.7%)
2	--	1 (0.8%)
Cancer Stage at Screening		
I	30 (25.0%)	30 (25.2%)
II	58 (48.3%)	66 (55.5%)
III	32 (26.7%)	22 (18.5%)
IV	--	1 (0.8%)
Days from Diagnosis, mean (SD)	24.5 (18.08)	20.9 (13.51)

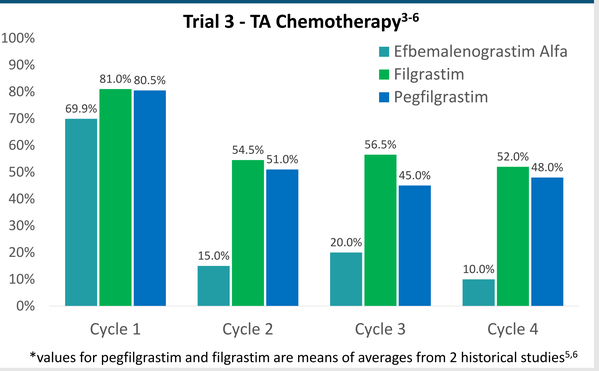
Trial 3[4] TA Chemotherapy	Efbemalenograstim Alfa (n = 83)	Placebo (n = 39)
Age, mean years (SD)	50.8 (9.25)	51.5 (9.00)
Baseline ECOG PS		
0	46 (55.4%)	27 (69.2%)
1	37 (44.6%)	12 (30.8%)
2	--	--
Cancer Stage at Screening		
I	--	--
II	43 (51.8%)	21 (53.8%)
III	22 (26.5%)	12 (30.8%)
IV	18 (21.7%)	6 (15.4%)

ECOG Eastern Cooperative Oncology Group; *PS* Performance Status; *SD* Standard Deviation; *TC* docetaxel + cyclophosphamide; *EC* epirubicin + cyclophosphamide; *TA* high myelotoxic docetaxel + doxorubicin (TA)

INCIDENCE OF SEVERE NEUTROPENIA







*values for pegfilgrastim and filgrastim are means of averages from 2 historical studies[5,6]

KEY TAKEAWAYS & CONCLUSIONS

- **Efbemalenograstim alfa is a novel, non-PEGylated, long-acting G-CSF containing two human G-CSFs fused with human IgG2-FC via a short peptide linker. This structure permits once-per-cycle administration for the reduction of chemotherapy-induced neutropenia.**
- **This analysis assessed the incidence of severe neutropenia (ISN; grade 4, ANC $<0.5 \times 10^9$/L) across all chemotherapy cycles in previous trials of efbemalenograstim alfa and different chemotherapy regimens in patients with stage I-III invasive breast cancer.**
- **Across studies, non-PEGylated efbemalenograstim alfa has demonstrated equivalent or lower incidence rates of severe neutropenia (grade 4, ANC $<0.5 \times 10^9$/L) during the first cycle of three types of chemotherapy (TC, EC and TA) and importantly, significantly lower rates in later cycles when compared to pegfilgrastim and filgrastim.**
- **These findings demonstrate that efbemalenograstim alfa may be more effective at preventing severe, life-threatening neutropenia at later chemotherapy cycles, which has meaningful implications for real-world breast cancer patients that are likely to receive chemotherapy for longer durations.**
- **Efbemalenograstim alfa (Ryzneuta, Acrotech Biopharma), FDA approved on November 22, 2023, is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.**

References: 1. Li S, Hou D, Wang C: Efbemalenograstim alfa, a long-acting granulocyte colony-stimulating factor, a novel dimeric G-CSF Fc fusion protein for reducing the risk of febrile neutropenia following chemotherapy. J Clin Exp Hematol 2:10-12, 2023; 2. Glaspy JA, et al. Efbemalenograstim Alfa, a Long-Acting Granulocyte Colony-Stimulating Factor Fusion Protein Without PEGylation, Versus Pegfilgrastim for Management of Chemotherapy-Induced Neutropenia in Patients With Breast Cancer: Results of a Phase III Randomized Noninferiority Trial. JCO Oncol Adv 2, e2400074(2025). 3. Zhang Q, et al. A randomized, multicenter phase III Study of once-per-cycle administration of efbemalenograstim alfa (F-627), a novel long-acting rhG-CSF, for prophylaxis of chemotherapy-induced neutropenia in patients with breast cancer. BMC Cancer. 2024 Sep 13;24(1):1143.; 4. Glaspy J, et al. Efbemalenograstim alfa, an Fc fusion protein, long-acting granulocyte-colony stimulating factor for reducing the risk of febrile neutropenia following chemotherapy: results of a phase III trial. Support Care Cancer. 2023 Dec 16;32(1):34.; 5. Green MD, et al. A randomized double-blind multicenter phase III study of fixed-dose single-administration pegfilgrastim versus daily filgrastim in patients receiving myelosuppressive chemotherapy. Ann Oncol. 2003;14(1):29–35.; 6. Holmes F: Blinded, randomized, multicenter study to evaluate single administration pegfilgrastim once per cycle versus daily filgrastim as an adjunct to chemotherapy in patients with high-risk stage II or stage III/IV breast cancer. J Clin Oncol 20:727-731, 2002

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