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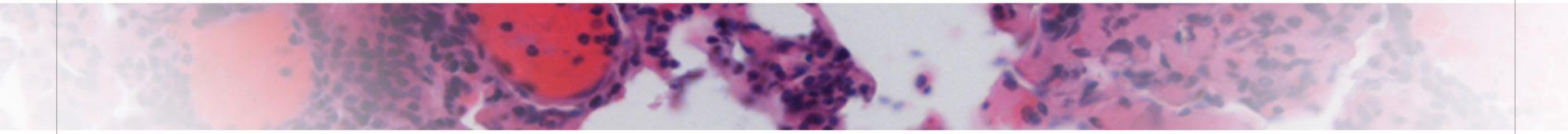

Mavorixafor for Patients With Chronic Neutropenic Disorders: Results From a Phase 1b, Open-Label, Multicenter Study

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Mavorixafor is an investigational product and the safety and efficacy have not been established. The investigational uses presented here have not been filed with or approved by the FDA or other regulatory authority.

FDA, US Food and Drug Administration.

Chronic Neutropenic Disorders

Chronic neutropenia
Blood disorders characterized by low levels of neutrophils (ANC <1500/µl for >3 months)[1,2]

Causes of chronic neutropenia

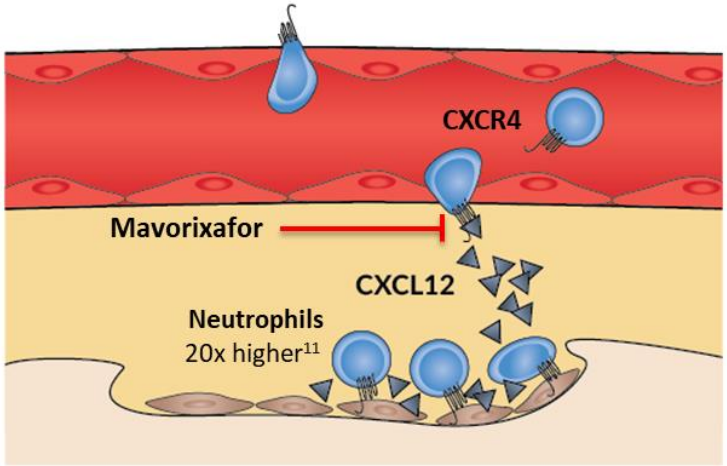
CN Disorders	Characterized by
CIN	Persistent neutropenia of unknown underlying cause and may overlap with autoimmune neutropenia[3]
Congenital	Genetic variants[4]
Cyclic	Recurrent neutropenia with episodes repeating typically every 3 weeks[5]

- Injectable G-CSF is the only approved therapy for severe chronic neutropenia[1,6]
- The CXCL12/CXCR4 axis is important for retention and mobilization of mature neutrophils from BM into the blood[7,8]

Targeting CXCR4 may provide an effective strategy for treatment of patients with CN disorders

ANC, absolute neutrophil count; **BM,** bone marrow; **CN**, chronic neutropenic; **CIN**, chronic idiopathic neutropenia; **CXCL12**, C-X-C chemokine ligand 12; **CXCR4**, C-X-C chemokine receptor 4; **G-CSF**, granulocyte colony–stimulating factor.

Mavorixafor Is an Oral CXCR4 Antagonist Being Evaluated in Clinical Trials for Chronic Neutropenic Disorders



Mavorixafor antagonizes CXCL12/CXCR4 leading trafficking of neutrophils from the BM to blood[8,9]

- High potency and selectivity[12]
- Once-daily oral dosing[12]
- Increases peripheral neutrophil count in a phase 2 trial of participants with WHIM syndrome[12,13]
- Well tolerated (safety information from >200 participants[12])

BM, bone marrow; **CXCL12**, C-X-C chemokine ligand 12; **CXCR4**, C-X-C chemokine receptor 4; **WHIM**, Warts, Hypogammaglobulinemia, Infections, and Myelokathexis.

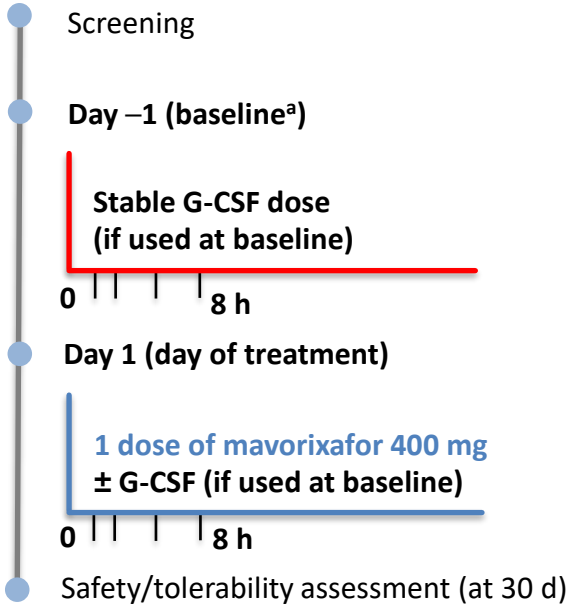
Here, we report the findings of phase 1b, open-label, multicenter trial (NCT04154488) evaluating the safety, tolerability, and proof of concept for efficacy, of mavorixafor alone or with concurrent G-CSF use across several CN disorders[14,a]

CN, chronic neutropenic**; G-CSF**, granulocyte colony–stimulating factor.

[a]Results shown in this presentation include participants from 2 different studies all of whom who were given mavorixafor. The results after first dose of mavorixafor on Day 1 are being presented.

A Phase 1b Trial Evaluating Safety and Tolerability of Mavorixafor in Chronic Neutropenic Disorders

Trial Design



- Multiple ANC assessments were done between 0 and 8 hours on Day –1 and Day 1

Key Eligibility Criteria

- Aged ≥12 years
- Diagnosed with CIN, congenital, or cyclic neutropenia ≥6 months prior and either ANC <1000/µL at screening visits or on G-CSF

ANC, absolute neutrophil count; **CIN**, chronic idiopathic neutropenia; **G-CSF**, granulocyte colony–stimulating factor.

[a]Baseline is defined as the average value over 6–8 hours on Day –1 Visit. If Day –1 assessment is not done, baseline is defined as the last nonmissing value prior to the first dose of mavorixafor.

A Phase 1b Trial Evaluating Safety and Tolerability of Mavorixafor in Chronic Neutropenic Disorders (cont'd)

Endpoints and Assessments

Primary endpoints

- Change and fold change from Day –1 in ANC levels over 6–8 hours on Day 1
- Incidence and severity of TEAEs

Subgroup analyses

- Mean change and peak increase in ANC levels for:
  - Participants not on G-CSF
  - Participants on G-CSF (dosed at the same time as mavorixafor)

Assessments

- Peripheral blood WBC, ANC, ALC, and AMC levels collected pre-dose and every 1-2 hours for 8 hours

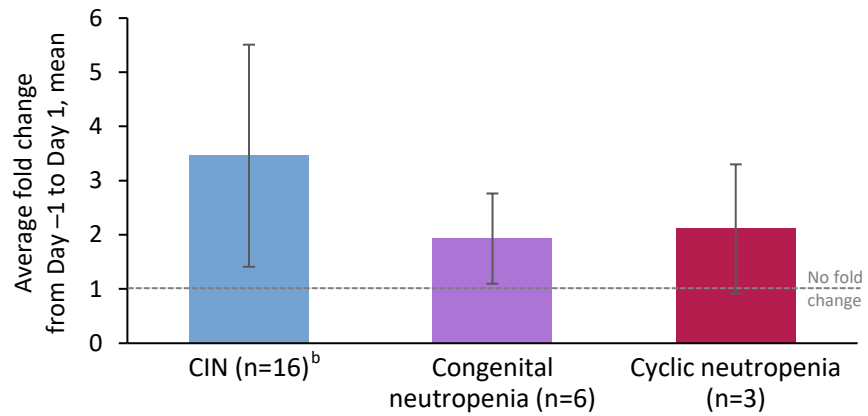
26 participants were enrolled; 25 had ≥1 post-dose lab assessments (data cutoff July 26, 2022)[b]

ALC, absolute lymphocyte count**; AMC,** absolute monocyte count**; ANC**, absolute neutrophil count; **CIN**, chronic idiopathic neutropenia; **CN**, chronic neutropenic; **G-CSF**, granulocyte colony–stimulating factor; **TEAE**, treatment-emergent adverse event; **WBC**, white blood cell.

[a]Baseline is defined as the average value over 6–8 hours on Day –1 Visit. If Day –1 assessment is not done, baseline is defined as the last nonmissing value prior to the first dose of mavorixafor. [b]Of the 26 participants enrolled in the trial; 1 participant refused dosing with mavorixafor.

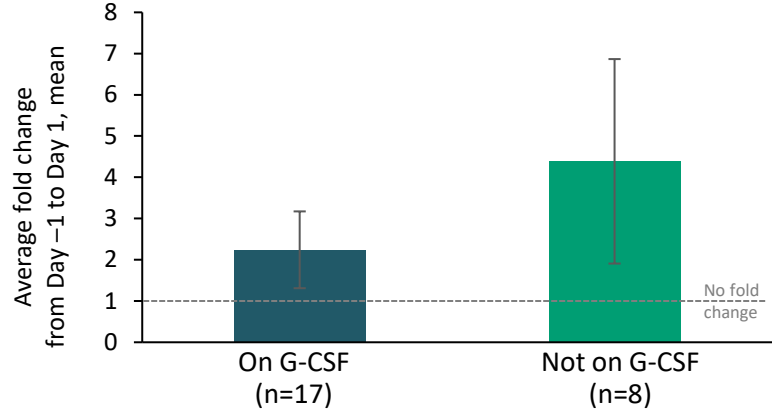
Fold Change in ANC Levels After Single Dose of Mavorixafor

Change in ANC Levels by Type of CN Disorders (N=25)[a,b]



	CIN (n=16)	Congenital (n=6)	Cyclic (n=3)
Patients with fold change ≥2, n (%)	15 (93.8)	4 (66.7)	2 (66.7)

Change in ANC Levels by G-CSF Use (N=25)[a,b]



	On G-CSF (n=17)	Not on G-CSF (n=8)
Patient with fold change ≥2, n (%)	13 (76.5)	8 (100.0)

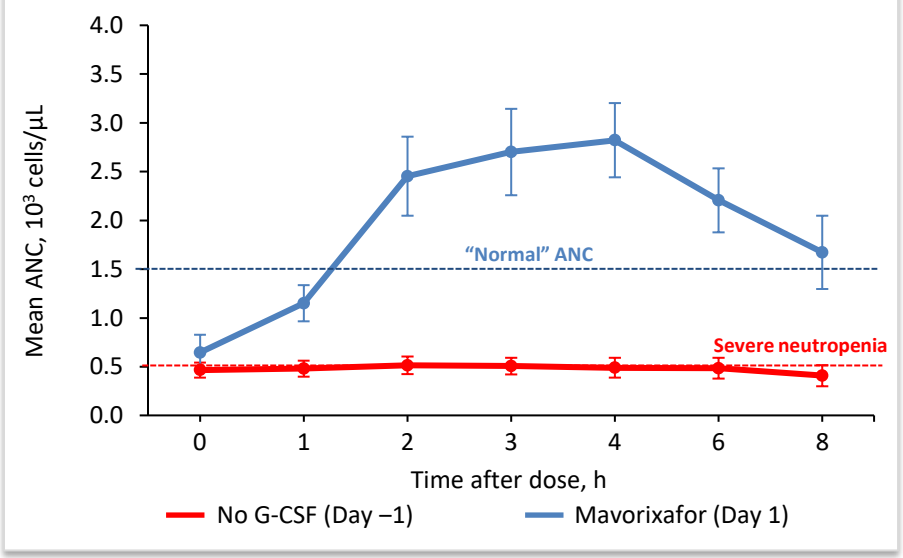
ANC, absolute neutrophil count**; CIN,** chronic idiopathic neutropenia**; CN,** chronic neutropenic**; G-CSF**, granulocyte colony–stimulating factor.

Data cutoff July 26, 2022.

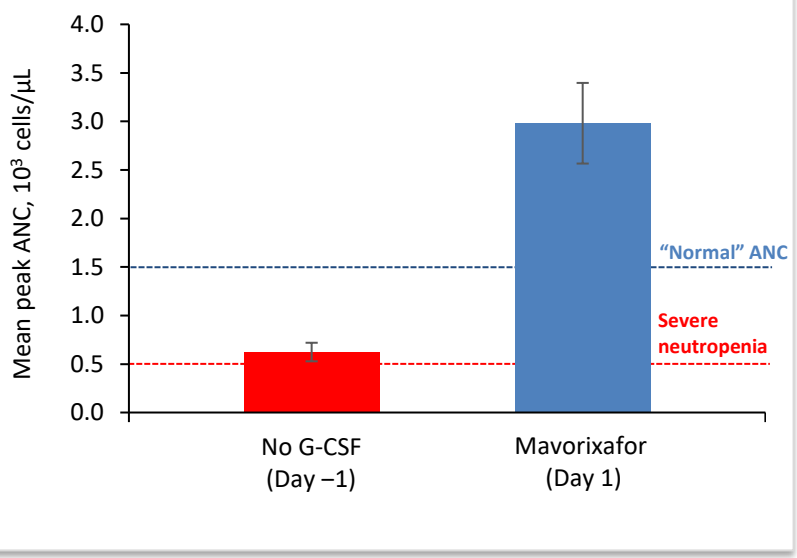
[a]Error bars represent standard deviation. [b]Significant from 0 at alpha level of 0.05 based on 2-sample *t* test.

Absolute ANC Change for Participants Not on G-CSF[a]

Mean ANC (n=7)[b]



Mean Peak ANC (n=7)[b]



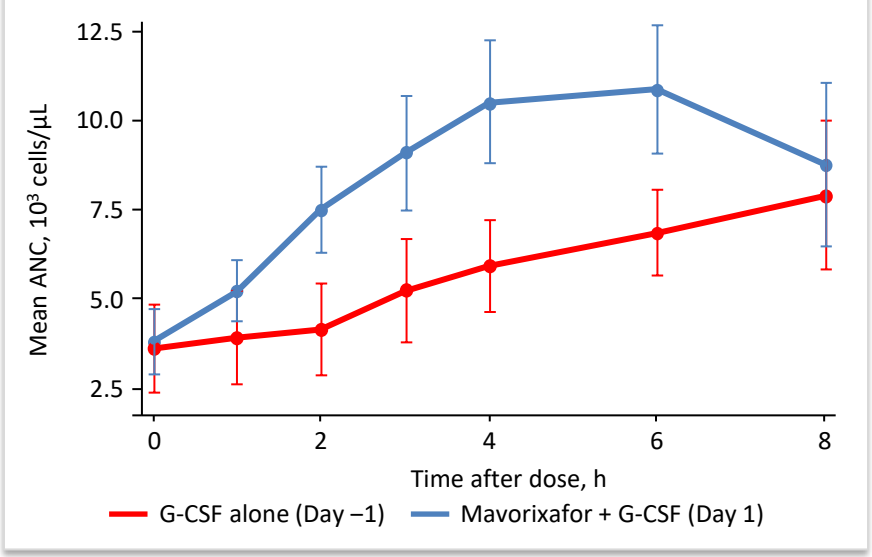
ANC, absolute neutrophil count; **G-CSF**, granulocyte colony–stimulating factor.

Data cutoff July 26, 2022.

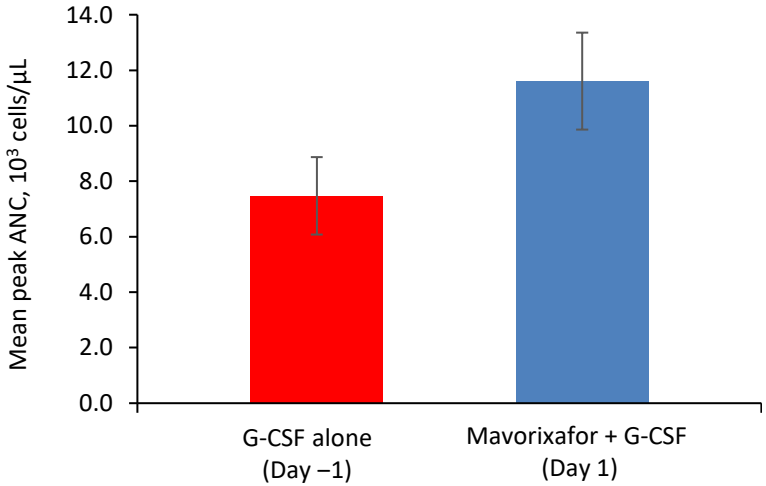
[a]Participants with neutropenia were defined as having ANC <1500 cell/µL. [b]Error bars represent 1 unit of standard error of the mean.

Absolute ANC Change for Participants on G-CSF (Dosed in the Morning)

Mean ANC (n=9)[a,b]



Mean Peak ANC (n=9)[a,b]



ANC, absolute neutrophil count**; G-CSF**, granulocyte colony–stimulating factor.

Data cutoff July 26, 2022.

[a]Error bars represent 1 unit of standard error of the mean. [b]The G-CSF dose, schedule, and hour for administration were not part of the protocol. Some participants received G-CSF every other day or less frequently, and some participants received G-CSF the night before mavorixafor per their normal dosing schedule.

Safety Summary

TEAEs (N=65)[a,b]

AE Toxicity Grade	Events, n (%)
1	53 (81.5)
2	11 (16.9)
3	1 (1.5)

Data rounded up to 1 decimal place.

- Majority of AEs (98.5%) were mild or moderate
- Grade 3 AE neutropenic typhlitis was not related to the treatment
- No treatment-related serious AEs were reported

Mavorixafor-Related TEAEs (N=51)[c]

AE Terms[b]	AE Count, n (%)
CTCAE Grade 1	**42 (82.4)**
Diarrhea	6 (14.3)
Fatigue	3 (7.1)
Functional dyspepsia from not fasting	3 (7.1)
Nausea	2 (4.8)
Dizziness	2 (4.8)
Other[c]	26 (61.9)
CTCAE Grade 2	**9 (17.6)**
Nausea	2 (22.2)
Other[c]	7 (77.8)

Data rounded up to 1 decimal place.

AE, adverse event**; CTCAE**, Common Terminology Criteria for Adverse Events; **TEAE**, treatment-emergent adverse event.

Data cutoff July 26, 2022.

[a]Only AEs with completed CTCAE grading (v5.0) assessments at the time of the data cutoff are included. [b]Combined coded terms and verbatim terms. [c]Mavorixafor-related TEAEs with counts >1 are shown.

Conclusions

- Observe a meaningful increase in ANC after treatment with a single dose of mavorixafor
- Responses were seen across the types of CN disorders and G-CSF use
- Mavorixafor was overall well tolerated
- Our findings support further exploration of mavorixafor in treatment of CN disorders beyond WHIM syndrome

ANC, absolute neutrophil count; **CN**, chronic neutropenic; **G-CSF**, granulocyte colony–stimulating factor; **WHIM**, Warts, Hypogammaglobulinemia, Infections, and Myelokathexis.

Based on these encouraging early efficacy results, the phase 1b trial has been expanded to evaluate up to 25 additional participants with longer treatment duration (6 months).

For more information, please see https://clinicaltrials.gov/ct2/show/NCT04154488

Contact: clinicaltrialinfo@x4pharma.com

CN, chronic neutropenic.

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Questions?

For full clinical trial details, visit ClinicalTrials.gov identifier: NCT04154488.
https://clinicaltrials.gov/ct2/show/NCT04154488

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