About the GENESIS Trial

The GENESIS trial (NCT03246529) is a 2-part, Phase–3, randomized, double-blind, placebo-controlled, multicenter study evaluating the safety and efficacy of APHEXDA™ (motixafortide) plus filgrastim (G-CSF), compared to placebo plus filgrastim, for the mobilization of hematopoietic stem cells (HSC) for autologous transplantation in multiple myeloma patients.[1]

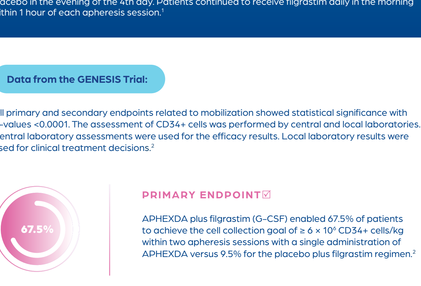
Part 1 was a single center, lead-in, open-label study involving 12 patients treated with motixafortide plus filgrastim designed to ascertain the dose. Part 2 involved 122 patients who were randomized 2:1 in a double-blind, placebo-controlled, multicenter study.[1]

The primary objective of Part 2 was to evaluate if one dose of motixafortide plus filgrastim is superior to placebo plus filgrastim in the ability to mobilize ≥ 6 million CD34+ cells in up to two apheresis sessions.[1] A key secondary objective of the study was to evaluate if one dose of motixafortide plus filgrastim is superior to placebo plus filgrastim in the ability to mobilize ≥ 6 million CD34+ cells in one apheresis session. Additional objectives included time to engraftment of neutrophils and platelets and durability of engraftment, as well as other efficacy and safety parameters.[1]

APHEXDA is contraindicated in patients with a history of serious hypersensitivity reactions to motixafortide.

Please see the Important Safety Information at the end of this study synopsis and the full Prescribing Information.

Trial Design: Part 2

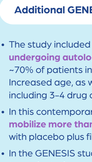


A total of 122 multiple myeloma patients from 18 sites in 5 countries were enrolled and randomized 2:1 to receive either motixafortide plus filgrastim (80 patients) or placebo plus filgrastim (42 patients) for HSC mobilization.[1]

All patients received 10–15 mcg/kg filgrastim in the morning for 4 days before receiving APHEXDA or placebo in the evening of the 4th day. Patients continued to receive filgrastim daily in the morning within 1 hour of each apheresis session.[1]

Data from the GENESIS Trial:

All primary and secondary endpoints related to mobilization showed statistical significance with p-values <0.0001. The assessment of CD34+ cells was performed by central and local laboratories. Central laboratory assessments were used for the efficacy results. Local laboratory results were used for clinical treatment decisions.[2]

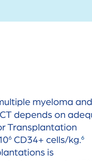


PRIMARY ENDPOINT

APHEXDA plus filgrastim (G-CSF) enabled 67.5% of patients to achieve the cell collection goal of ≥ 6 x 10^6 CD34+ cells/kg within two apheresis sessions with a single administration of APHEXDA versus 9.5% for the placebo plus filgrastim regimen.[2]

LOCAL LAB ASSESSMENT

86.3% of patients harvested at least 6 million stem cells after one dose and one apheresis session in the APHEXDA treatment arm versus 9.5% in the placebo arm (as measured by local laboratory data).[3,*]



** Local laboratory data were used for sensitivity analysis. Data are descriptive, not statistically powered, and not prespecified. The information should be cautiously interpreted.*

SAFETY

Motixafortide plus filgrastim was well tolerated with the most common treatment-emergent adverse events observed being transient, grade 1/2 injection site reactions. Among 92 patients with multiple myeloma who received at least one dose of APHEXDA 1.25 mg/kg subcutaneously plus filgrastim, serious adverse reactions occurred in 5.4% of patients receiving APHEXDA plus filgrastim. Serious adverse reactions included vomiting, injection site reaction, hypersensitivity reaction, injection site cellulitis, hypokalemia and hypoxia. The most common adverse reactions occurring in GENESIS (incidence >20%) were injection site reactions (pain, erythema and pruritus), pruritus, flushing, and back pain.[2]

Additional GENESIS Data:

- The study included **patients that are representative of the typical multiple myeloma population undergoing autologous stem cell transplantation (ASCT)**, with a median age of 63 years and with ~70% of patients in both arms of the trial receiving lenalidomide-containing induction therapy. Increased age, as well as increased exposure to lenalidomide-containing induction regimens, including 3–4 drug combination regimens, have been associated with impaired HSC mobilization.[1]
- In this contemporary population, **patients in the APHEXDA plus filgrastim arm were able to mobilize more than four times the amount of stem cells** in a single apheresis session compared with placebo plus filgrastim.[2]
- In the GENESIS study, time to neutrophil and platelet engraftment and graft durability following transplantation were similar across treatment groups.[2]

A planned interim analysis by the independent Data Monitoring Committee (DMC) revealed statistically significant benefit with motixafortide plus filgrastim, leading to immediate early cessation of patient enrollment at 122, without the need to recruit 177 patients as originally planned.[4]

Autologous stem cell transplantation (ASCT):

Autologous stem cell transplantation (ASCT) is part of the standard of care for multiple myeloma and delivers prolonged survival for patients with this cancer type.[5] The success of ASCT depends on adequate mobilization of stem cells during the treatment process. The American Society for Transplantation and Cellular Therapy (ASTCT) guidelines recommends collection target of 3–5 x 10^6 CD34+ cells/kg.[6] Additionally, collection of a sufficient number of stem cells to perform two transplantations is recommended.[6–8] Historically, depending on induction regimens and mobilization strategies, up to 47% of patients have had challenges collecting target numbers of hematopoietic stem cells for ASCT after one apheresis session.[9–10]

APHEXDA Indication and Important Safety Information

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION

APHEXDA is indicated in combination with filgrastim (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with multiple myeloma.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

APHEXDA is contraindicated in patients with a history of serious hypersensitivity reactions to motixafortide.

WARNINGS AND PRECAUTIONS

- **Anaphylactic Shock and Hypersensitivity Reactions:** Anaphylactic shock and hypersensitivity reactions have occurred. Premedicate all patients with a triple drug premedication regimen that includes an H1-antihistamine, an H2 blocker, and a leukotriene inhibitor approximately 30–60 minutes prior to each dose of APHEXDA. Administer APHEXDA in a setting where personnel and therapies are immediately available for treatment of anaphylaxis and other systemic reactions. Monitor patients for 1 hour following APHEXDA administration and manage reactions promptly. Patients receiving negative chronotropic drugs (e.g., beta-blockers) may be more at risk for hypotension in the event of a hypersensitivity reaction and these drugs, when appropriate, should be replaced with non-chronotropic drugs.
- **Injection Site Reactions:** Injection site reactions (73%) including pain (53%), erythema (27%), and pruritus (24%) have occurred. Severe reactions occurred in 9% of patients. Premedicate with an analgesic premedication (e.g., acetaminophen) prior to each APHEXDA dose. Use analgesic medication and local treatments post-dose, as needed.
- **Tumor Cell Mobilization in Patients with Leukemia:** For the purpose of hematopoietic stem cell (HSC) mobilization, APHEXDA may cause mobilization of leukemic cells and subsequent contamination of the apheresis product. Therefore, APHEXDA is not intended for HSC mobilization and harvest in patients with leukemia.
- **Leukocytosis:** Administering APHEXDA in conjunction with filgrastim increases circulating leukocytes as well as HSC populations. Monitor white blood cell counts during APHEXDA use.
- **Potential for Tumor Cell Mobilization:** When APHEXDA is used in combination with filgrastim for HSC mobilization, tumor cells may be released from the marrow and subsequently collected in the leukapheresis product. The effect of potential reinfusion of tumor cells has not been well-studied.
- **Embryo–fetal Toxicity:** Based on its mechanism of action, APHEXDA can cause fetal harm. Advise pregnant women of the potential risk to the fetus. Verify pregnancy status in females of reproductive potential prior to initiating treatment with APHEXDA and advise use of effective contraception during treatment and for 8 days after the final dose.

ADVERSE REACTIONS

The most common adverse reactions (incidence >20%) in patients treated with APHEXDA were injection site reactions (73%, including pain (53%), erythema (27%), pruritus (24%)); pruritus (38%); flushing (33%); back pain (21%).

USE IN SPECIFIC POPULATIONS

Pregnancy: Please see the important information in Warnings and Precautions under Embryo-fetal Toxicity.
Lactation: There are no data on the presence of motixafortide in human milk, the effects on the breastfed child, or the effects on milk production. Advise females that breastfeeding is not recommended during treatment with APHEXDA and for 8 days after the final dose.
Pediatric Use: The safety and effectiveness of APHEXDA have not been established in pediatric patients.

Please see the accompanying full **Prescribing Information**.

bioLineRx

Israel Headquarters
Modi'in Technology Park
2 HaMarpeh Street
Modi'in 7177871, Israel
+972-8-642-9100

U.S. Operations
CityPoint
77 Fourth Avenue
Waltham, MA 02451 USA
+1-617-859-6409

Email: info@BioLineRx.com
Web: https://www.biolinerx.com
LinkedIn: @BioLineRx
Twitter: @BioLineRx_Ltd

1. Cress, ZD, et al Future Oncology. 2019;15(30):3555–3563.
2. APHEXDA™ Prescribing Information. BioLineRx Ltd., Modi'in, Israel. 2023.
3. BioLineRx. Data on File #1005. June 29, 2023.
4. Cress ZD, et al. Nature Medicine. 2023;29(4):869–879.
5. Kumar SK, et al. Blood. 2008;111(5):2516–2520.
6. Giralt S, et al. Biol Blood Marrow Transplant. 2014;20(3):295–308.
7. Giralt S, et al. Leukemia. 2009;23(10):1904–1912.
8. Giralt S, et al. Biol Blood Marrow Transplant. 2015;21(12):2039–2051.
9. Edmsson J, et al. Poster presented at: 64th American Society of Hematology Annual Meeting and Exposition; December 10–13, 2022; New Orleans, LA.
10. DiPersio JF, et al. Blood. 2009;113(23):5720–6.

US-COBP-2300012 (V1.0) 09/2023