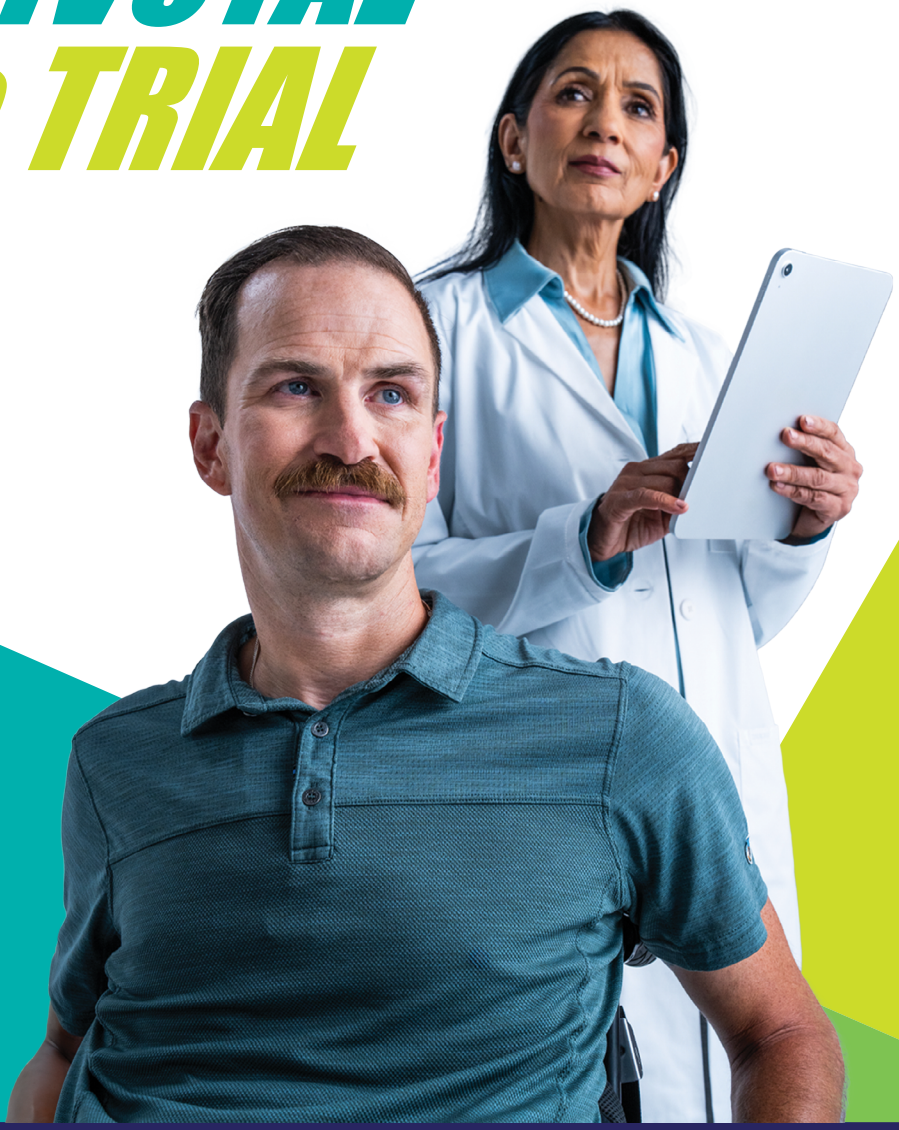
The First and Only FDA-Approved Treatment for Friedreich Ataxia (FA) in Patients 16 Years and Older[1]

RESULTS FROM THE PIVOTAL MOXIe TRIAL

SKYCLARYS® (omaveloxolone) 50 mg capsules



Chris, age 42

Outdoorsman

Taking SKYCLARYS since 2023

Patients featured are paid spokespersons for Biogen.

INDICATION

- SKYCLARYS® (omaveloxolone) is indicated for the treatment of Friedreich ataxia in adults and adolescents aged 16 years and older

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Elevation of Aminotransferases

- Treatment with SKYCLARYS can cause an elevation in hepatic transaminases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]). The incidence of elevations of ALT or AST above 5 times and 3 times the upper limit of normal (ULN) was 16% and 31%, respectively, in patients treated with SKYCLARYS. There were no cases of concomitant elevation of transaminases and total bilirubin observed. Maximum increases in ALT and AST occurred within 12 weeks after starting SKYCLARYS. Increases in serum aminotransferases were generally asymptomatic and reversible following discontinuation of SKYCLARYS

Please see additional Important Safety Information throughout and full Prescribing Information.

SKYCLARYS WAS SHOWN TO SLOW DISEASE PROGRESSION

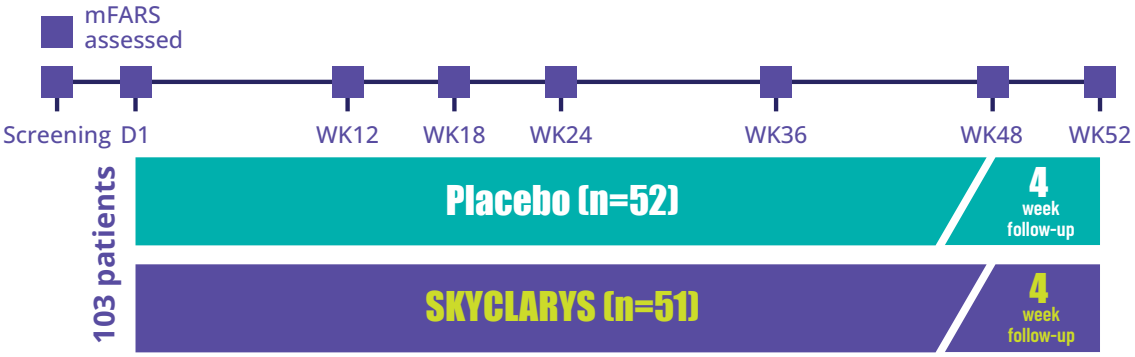
SKYCLARYS® (omaveloxolone) 50 mg capsules

The MOXIe trial was the largest clinical trial of its kind in FA

The MOXIe trial was an international, double-blind, randomized, placebo-controlled, multicenter, registrational phase 2 trial. A total of 103 patients with genetically confirmed diagnoses were randomized in a ratio of 1:1 (the All Randomized Population) to receive SKYCLARYS 150 mg once daily (n=51) or placebo (n=52).[1,2]

- 103 patients
- 11 institutions
- 3 continents
- 16 to 40 years of age
- 20 to 80 baseline mFARS score
- 53% male

The prespecified primary analysis was the change from baseline in the modified Friedreich Ataxia Rating Scale (mFARS) score compared with placebo at Week 48[2]



IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Elevation of Aminotransferases (cont'd)

- Monitor ALT, AST, and total bilirubin prior to initiation of SKYCLARYS, every month for the first 3 months of treatment, and periodically thereafter. If transaminases increase to levels greater than 5 times the ULN, or greater than 3 times the ULN with evidence of liver dysfunction (e.g., elevated bilirubin), immediately discontinue SKYCLARYS and repeat liver function tests as soon as possible. If transaminase levels stabilize or resolve, SKYCLARYS may be reinitiated with an appropriate increased frequency of monitoring of liver function

Elevation of B-Type Natriuretic Peptide

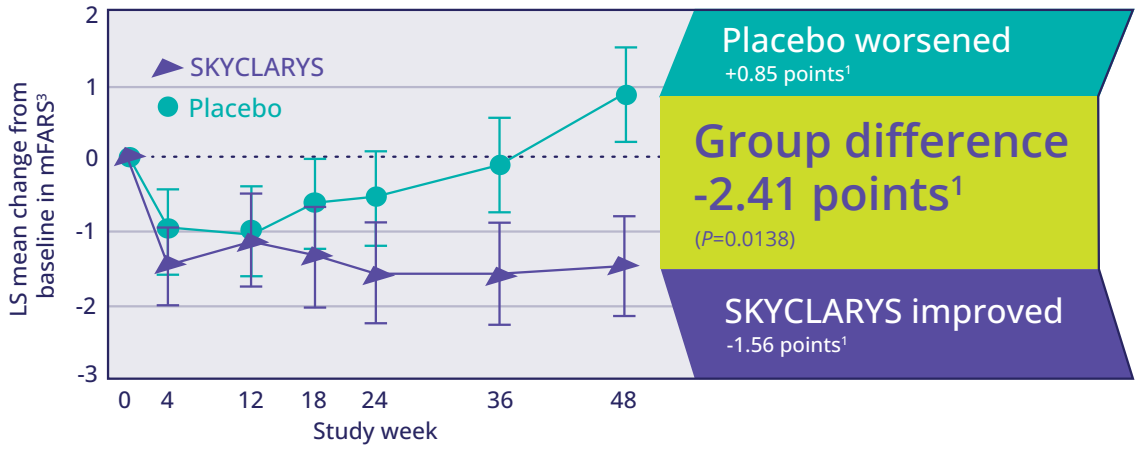
- Treatment with SKYCLARYS can cause an increase in B-type natriuretic peptide (BNP), a marker of cardiac function. A total of 14% of patients treated with SKYCLARYS had an increase from baseline in BNP value above the ULN (100 pg/mL), compared to 4% of patients who received placebo. The incidence of elevation of BNP above 200 pg/mL was 4% in patients treated with SKYCLARYS. Cardiomyopathy and cardiac failure are common in patients with Friedreich ataxia. Whether the elevations in BNP are related to SKYCLARYS or cardiac disease associated with Friedreich ataxia is unclear
- Elevations in BNP may indicate cardiac failure and should prompt an evaluation of cardiac function. Check BNP prior to initiation of SKYCLARYS. Monitor patients for the signs and symptoms of fluid overload, such as sudden weight gain (3 pounds or more of weight gain in one day, or 5 pounds or more of weight gain in a week), peripheral edema, palpitations, and shortness of breath. If signs and symptoms of fluid overload develop, worsen, or require hospitalization, evaluate BNP and cardiac function, and manage appropriately. Management of fluid overload and heart failure may require discontinuation of SKYCLARYS

Please see additional Important Safety Information throughout and full Prescribing Information.

SKYCLARYS WAS SHOWN TO SLOW DISEASE PROGRESSION (cont'd)

SKYCLARYS® (omaveloxolone) 50 mg capsules

SKYCLARYS slowed disease progression in the MOXIe trial[1]



SKYCLARYS (n)	40	40	40	38	36	35	34
Placebo (n)	42	42	42	41	41	41	41

In the Full Analysis Population of patients without pes cavus (n=82).

Treatment with SKYCLARYS resulted in less physical impairment relative to placebo at Week 48[1]

Results from patient subgroups numerically favored SKYCLARYS over placebo regardless of[2]:

- **Age**
- **Sex**
- **GAA repeat length**
- **Ambulatory status**
- **Presence of pes cavus**

All 4 components of the mFARS assessment numerically favored SKYCLARYS over placebo.[2]

The greatest effects were on upper limb coordination, which has been linked to the ability to perform many activities of daily living, followed by upright stability, which defines important clinical milestones such as loss of ambulation.[4,5]

The MOXIe trial was not powered to detect a statistically significant difference among subgroups.[2]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Lipid Abnormalities

- Treatment with SKYCLARYS can cause changes in cholesterol. In Study 1, 29% of patients treated with SKYCLARYS reported elevated cholesterol above ULN at one or more time points. Mean increases were observed within 2 weeks of initiation of SKYCLARYS and returned to baseline within 4 weeks of discontinuing treatment. A total of 16% of patients treated with SKYCLARYS had an increase in low-density lipoprotein cholesterol (LDL-C) from baseline, compared to 8% of patients who received placebo. The mean increase in LDL-C for all SKYCLARYS-treated patients was 23.5 mg/dL at 48 weeks. A total of 6% of patients treated with SKYCLARYS had decreases in high-density lipoprotein cholesterol (HDL-C) from baseline compared to 4% of patients who received placebo. The mean decrease in HDL-C for all SKYCLARYS-treated patients was 5.3 mg/dL at 48 weeks
- Assess lipid parameters prior to initiation of SKYCLARYS and monitor periodically during treatment. Manage lipid abnormalities according to clinical guidelines

Please see additional Important Safety Information throughout and full Prescribing Information.

MORE THAN 2000 PATIENTS HAVE BEEN PRESCRIBED SKYCLARYS WORLDWIDE*[6]

SKYCLARYS® (omaveloxolone) 50 mg capsules

Start giving your patients a chance to slow FA progression with SKYCLARYS. Visit www.SkyclarysHCP.com to learn how.

Adverse reactions reported in ≥10% of patients treated with SKYCLARYS and greater than placebo[1]

Adverse reactions	SKYCLARYS (n=51)	Placebo (n=52)
Elevated liver enzymes (AST/ALT)	37%	2%
Headache	37%	25%
Nausea	33%	13%
Abdominal pain	29%	6%
Fatigue	24%	14%
Diarrhea	20%	10%
Musculoskeletal pain	20%	15%
Oropharyngeal pain	18%	6%
Influenza	16%	6%
Vomiting	16%	12%
Muscle spasms	14%	6%
Back pain	13%	8%
Decreased appetite	12%	4%
Rash	10%	4%

AST=aspartate aminotransferase; ALT=alanine aminotransferase.
*Based on commercial patients, early access patients, and clinical trial participants through July 2024.

Libby, age 27
Interior designer
Taking SKYCLARYS since 2023

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IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS
- The most common adverse reactions in Study 1 (≥20% and greater than placebo) were elevated liver enzymes (AST/ALT), headache, nausea, abdominal pain, fatigue, diarrhea, and musculoskeletal pain

DRUG INTERACTIONS
- Avoid concomitant use of SKYCLARYS with moderate or strong CYP3A4 inhibitors. If use cannot be avoided, dosage modifications are recommended
- Avoid concomitant use of SKYCLARYS with moderate or strong CYP3A4 inducers
- Refer to the prescribing information for dosing instructions for concomitant use of CYP3A4 and CYP2C8 substrates and monitor for lack of efficacy of the concomitant treatment
- Advise patients to avoid concomitant use with combined hormonal contraceptives, implants, and progestin only pills

SPECIFIC POPULATIONS

Pregnancy
- There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to SKYCLARYS during pregnancy. Healthcare providers are encouraged to enroll pregnant patients, or pregnant women may register themselves in the program by calling 1-866-609-1785 or by sending an email to SkyclarysPregnancySurveillance@ppd.com
- There are no adequate data on the development risks associated with the use of SKYCLARYS in pregnant women

Lactation
- There are no data on the presence of omaveloxolone or its metabolites in human milk. The effects on milk production and the breastfed infant are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SKYCLARYS and any potential adverse effects on the breastfed infant from SKYCLARYS or from the underlying maternal condition

Hepatic Impairment
- Avoid treatment with SKYCLARYS in patients with severe hepatic impairment, including those who develop severe hepatic impairment
- Reduced dosage in patients with moderate hepatic impairment with close monitoring for adverse reactions is recommended

Please see additional Important Safety Information throughout and full Prescribing Information.

References: 1. Skyclarys. Prescribing information. Biogen; 2024. **2.** Lynch DR, Chin MP, Delatycki MB, et al. Safety and efficacy of omaveloxolone in Friedreich ataxia (MOXIe study). *Ann Neurol.* 2021;89(2):212-225. **3.** Data on file. Biogen, 2022. **4.** Errors in text and figure 2B. Correction. *Ann Neurol*. 2023;94(6):1190. **5.** Rummey C, Farmer JM, Lynch DR. Predictors of loss of ambulation in Friedreich's ataxia. *EClinicalMedicine*. 2020;18:100213. **6.** Data on file. Biogen, 2024.

Intended for a US HCP audience.

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