

Omaveloxolon (Skyclarys™)

Biogen GmbH

Anhang 4-I zu Modul 4A und 4B

*Behandlung der Friedreich-Ataxie (FA) bei
Erwachsenen und Jugendlichen ab 16 Jahren*

Stand: 01.07.2025

Inhaltsverzeichnis

Krankheitsschwere (mFARS, 93 Punkte) - ITT-Population ohne schweren Pes cavus nach GAA1-Repeatlänge..	2
Krankheitsschwere (mFARS, 93 Punkte) - FAS-Population nach GAA1-Repeatlänge	3

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length ≥ 675 (Yes, No) - ITT Population without Pes Cavus

Page: 1 of 6

GAA1 repeat length ≥ 675 : Yes

	Placebo (N=18)	Omaveloxolone 150 mg (N=21)
Baseline		
N	18	21
Mean score	42.22	44.10
SD	12.445	10.329
Week 4		
N	18	21
LS mean change from baseline	-1.93	-1.31
SE	0.884	0.827
95% CI	(-3.70, -0.16)	(-2.97, 0.34)
LS mean difference (Omaveloxolone-Placebo)		0.62
SE		1.202
95% CI		(-1.79, 3.02)
p-value		0.6099
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		0.16
95% CI		(-0.47, 0.79)
Week 12		
N	18	21
LS mean change from baseline	-0.19	-1.61
SE	1.037	0.972
95% CI	(-2.27, 1.88)	(-3.55, 0.34)
LS mean difference (Omaveloxolone-Placebo)		-1.41
SE		1.410
95% CI		(-4.23, 1.41)
p-value		0.3211
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.31
95% CI		(-0.94, 0.32)

Note 1: LS Mean and Hedges' g are from the MMRM model for ITT population without Pes Cavus with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas **Data Tag:** FINAL **Run Date:** 02JUN2025

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length >=675 (Yes, No) - ITT Population without Pes Cavus

Page: 2 of 6

GAA1 repeat length >=675: Yes

	Placebo (N=18)	Omaveloxolone 150 mg (N=21)
Week 18		
N	18	20
LS mean change from baseline	-0.13	-1.36
SE	1.084	1.028
95% CI	(-2.29, 2.04)	(-3.42, 0.69)
LS mean difference (Omaveloxolone-Placebo)		-1.24
SE		1.483
95% CI		(-4.20, 1.73)
p-value		0.4078
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.26
95% CI		(-0.90, 0.38)
Week 24		
N	18	19
LS mean change from baseline	-0.08	-0.93
SE	0.994	0.959
95% CI	(-2.08, 1.91)	(-2.85, 0.99)
LS mean difference (Omaveloxolone-Placebo)		-0.85
SE		1.373
95% CI		(-3.60, 1.91)
p-value		0.5398
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.19
95% CI		(-0.84, 0.45)

Note 1: LS Mean and Hedges' g are from the MMRM model for ITT population without Pes Cavus with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas **Data Tag:** FINAL **Run Date:** 02JUN2025

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length >=675 (Yes, No) - ITT Population without Pes Cavus

Page: 3 of 6

GAA1 repeat length >=675: Yes

	Placebo (N=18)	Omaveloxolone 150 mg (N=21)
Week 36		
N	18	19
LS mean change from baseline	0.39	-1.78
SE	1.008	0.972
95% CI	(-1.63, 2.41)	(-3.72, 0.17)
LS mean difference (Omaveloxolone-Placebo)		-2.17
SE		1.392
95% CI		(-4.95, 0.62)
p-value		0.1253
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.49
95% CI		(-1.14, 0.16)
Week 48		
N	18	19
LS mean change from baseline	1.91	-2.20
SE	0.972	0.937
95% CI	(-0.04, 3.86)	(-4.08, -0.32)
LS mean difference (Omaveloxolone-Placebo)		-4.11
SE		1.343
95% CI		(-6.80, -1.41)
p-value		0.0035
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.96
95% CI		(-1.64, -0.28)

Note 1: LS Mean and Hedges' g are from the MMRM model for ITT population without Pes Cavus with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas **Data Tag:** FINAL **Run Date:** 02JUN2025

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length ≥ 675 (Yes, No) - ITT Population without Pes Cavus

Page: 4 of 6

GAA1 repeat length ≥ 675 : No

	Placebo (N=18)	Omaveloxolone 150 mg (N=11)
Baseline		
N	18	11
Mean score	34.88	38.95
SD	9.715	10.085
Week 4		
N	18	10
LS mean change from baseline	-0.82	-0.65
SE	0.899	1.172
95% CI	(-2.62, 0.98)	(-3.00, 1.70)
LS mean difference (Omaveloxolone-Placebo)		0.17
SE		1.426
95% CI		(-2.68, 3.03)
p-value		0.9039
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		0.05
95% CI		(-0.73, 0.82)
Week 12		
N	18	10
LS mean change from baseline	-1.04	0.54
SE	1.058	1.378
95% CI	(-3.16, 1.08)	(-2.22, 3.30)
LS mean difference (Omaveloxolone-Placebo)		1.58
SE		1.693
95% CI		(-1.81, 4.98)
p-value		0.3534
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		0.35
95% CI		(-0.43, 1.13)

Note 1: LS Mean and Hedges' g are from the MMRM model for ITT population without Pes Cavus with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas **Data Tag:** FINAL **Run Date:** 02JUN2025

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length >=675 (Yes, No) - ITT Population without Pes Cavus

Page: 5 of 6

GAA1 repeat length >=675: No

	Placebo (N=18)	Omaveloxolone 150 mg (N=11)
Week 18		
N	18	10
LS mean change from baseline	-0.17	-1.39
SE	1.107	1.440
95% CI	(-2.38, 2.05)	(-4.28, 1.49)
LS mean difference (Omaveloxolone-Placebo)		-1.23
SE		1.774
95% CI		(-4.78, 2.33)
p-value		0.4923
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.26
95% CI		(-1.03, 0.52)
Week 24		
N	18	10
LS mean change from baseline	0.06	-1.91
SE	1.015	1.320
95% CI	(-1.98, 2.09)	(-4.56, 0.73)
LS mean difference (Omaveloxolone-Placebo)		-1.97
SE		1.619
95% CI		(-5.22, 1.28)
p-value		0.2293
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.45
95% CI		(-1.24, 0.33)

Note 1: LS Mean and Hedges' g are from the MMRM model for ITT population without Pes Cavus with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas **Data Tag:** FINAL **Run Date:** 02JUN2025

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length >=675 (Yes, No) - ITT Population without Pes Cavus

Page: 6 of 6

GAA1 repeat length >=675: No

	Placebo (N=18)	Omaveloxolone 150 mg (N=11)
Week 36		
N	18	9
LS mean change from baseline	0.51	-1.62
SE	1.029	1.383
95% CI	(-1.55, 2.58)	(-4.39, 1.15)
LS mean difference (Omaveloxolone-Placebo)		-2.14
SE		1.683
95% CI		(-5.51, 1.24)
p-value		0.2097
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.49
95% CI		(-1.30, 0.32)
Week 48		
N	18	9
LS mean change from baseline	0.85	-1.00
SE	0.992	1.335
95% CI	(-1.14, 2.84)	(-3.68, 1.67)
LS mean difference (Omaveloxolone-Placebo)		-1.85
SE		1.620
95% CI		(-5.11, 1.40)
p-value		0.2576
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.44
95% CI		(-1.25, 0.37)

Note 1: LS Mean and Hedges' g are from the MMRM model for ITT population without Pes Cavus with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas **Data Tag:** FINAL **Run Date:** 02JUN2025

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length ≥ 675 (Yes, No) - FAS Population

Page: 1 of 6

GAA1 repeat length ≥ 675 : Yes

	Placebo (N=18)	Omaveloxolone 150 mg (N=21)
Baseline		
N	18	21
Mean score	42.22	44.10
SD	12.445	10.329
Week 4		
N	18	21
LS mean change from baseline	-1.93	-1.31
SE	0.884	0.827
95% CI	(-3.70, -0.16)	(-2.97, 0.34)
LS mean difference (Omaveloxolone-Placebo)		0.62
SE		1.202
95% CI		(-1.79, 3.02)
p-value		0.6099
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		0.16
95% CI		(-0.47, 0.79)
Week 12		
N	18	21
LS mean change from baseline	-0.19	-1.61
SE	1.037	0.972
95% CI	(-2.27, 1.88)	(-3.55, 0.34)
LS mean difference (Omaveloxolone-Placebo)		-1.41
SE		1.410
95% CI		(-4.23, 1.41)
p-value		0.3211
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.31
95% CI		(-0.94, 0.32)

Note 1: LS Mean and Hedges' g are from the MMRM model for FAS population with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas **Data Tag:** FINAL **Run Date:** 25JUN2024

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length >=675 (Yes, No) - FAS Population

Page: 2 of 6

GAA1 repeat length >=675: Yes

	Placebo (N=18)	Omaveloxolone 150 mg (N=21)
Week 18		
N	18	20
LS mean change from baseline	-0.13	-1.36
SE	1.084	1.028
95% CI	(-2.29, 2.04)	(-3.42, 0.69)
LS mean difference (Omaveloxolone-Placebo)		-1.24
SE		1.483
95% CI		(-4.20, 1.73)
p-value		0.4078
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.26
95% CI		(-0.90, 0.38)
Week 24		
N	18	19
LS mean change from baseline	-0.08	-0.93
SE	0.994	0.959
95% CI	(-2.08, 1.91)	(-2.85, 0.99)
LS mean difference (Omaveloxolone-Placebo)		-0.85
SE		1.373
95% CI		(-3.60, 1.91)
p-value		0.5398
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.19
95% CI		(-0.84, 0.45)

Note 1: LS Mean and Hedges' g are from the MMRM model for FAS population with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas Data Tag: FINAL Run Date: 25JUN2024

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length ≥ 675 (Yes, No) - FAS Population

Page: 3 of 6

GAA1 repeat length ≥ 675 : Yes

	Placebo (N=18)	Omaveloxolone 150 mg (N=21)
Week 36		
N	18	19
LS mean change from baseline	0.39	-1.78
SE	1.008	0.972
95% CI	(-1.63, 2.41)	(-3.72, 0.17)
LS mean difference (Omaveloxolone-Placebo)		-2.17
SE		1.392
95% CI		(-4.95, 0.62)
p-value		0.1253
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.49
95% CI		(-1.14, 0.16)
Week 48		
N	18	19
LS mean change from baseline	1.91	-2.20
SE	0.972	0.937
95% CI	(-0.04, 3.86)	(-4.08, -0.32)
LS mean difference (Omaveloxolone-Placebo)		-4.11
SE		1.343
95% CI		(-6.80, -1.41)
p-value		0.0035
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.96
95% CI		(-1.64, -0.28)

Note 1: LS Mean and Hedges' g are from the MMRM model for FAS population with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas Data Tag: FINAL Run Date: 25JUN2024

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length ≥ 675 (Yes, No) - FAS Population

Page: 4 of 6

GAA1 repeat length ≥ 675 : No

	Placebo (N=18)	Omaveloxolone 150 mg (N=10)
Baseline		
N	18	10
Mean score	34.88	39.60
SD	9.715	10.389
Week 4		
N	18	10
LS mean change from baseline	-0.82	-0.65
SE	0.899	1.172
95% CI	(-2.62, 0.98)	(-3.00, 1.70)
LS mean difference (Omaveloxolone-Placebo)		0.17
SE		1.426
95% CI		(-2.68, 3.03)
p-value		0.9039
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		0.05
95% CI		(-0.73, 0.82)
Week 12		
N	18	10
LS mean change from baseline	-1.04	0.54
SE	1.058	1.378
95% CI	(-3.16, 1.08)	(-2.22, 3.30)
LS mean difference (Omaveloxolone-Placebo)		1.58
SE		1.693
95% CI		(-1.81, 4.98)
p-value		0.3534
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		0.35
95% CI		(-0.43, 1.13)

Note 1: LS Mean and Hedges' g are from the MMRM model for FAS population with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas **Data Tag:** FINAL **Run Date:** 25JUN2024

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length >=675 (Yes, No) - FAS Population

Page: 5 of 6

GAA1 repeat length >=675: No

	Placebo (N=18)	Omaveloxolone 150 mg (N=10)
Week 18		
N	18	10
LS mean change from baseline	-0.17	-1.39
SE	1.107	1.440
95% CI	(-2.38, 2.05)	(-4.28, 1.49)
LS mean difference (Omaveloxolone-Placebo)		-1.23
SE		1.774
95% CI		(-4.78, 2.33)
p-value		0.4923
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.26
95% CI		(-1.03, 0.52)
Week 24		
N	18	10
LS mean change from baseline	0.06	-1.91
SE	1.015	1.320
95% CI	(-1.98, 2.09)	(-4.56, 0.73)
LS mean difference (Omaveloxolone-Placebo)		-1.97
SE		1.619
95% CI		(-5.22, 1.28)
p-value		0.2293
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.45
95% CI		(-1.24, 0.33)

Note 1: LS Mean and Hedges' g are from the MMRM model for FAS population with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas Data Tag: FINAL Run Date: 25JUN2024

MOXie Part 2: Modified Friedreich's Ataxia 93-points Rating Scale (mFARS) Total Score LS Mean Change from Baseline up to Week 48 by Visit from MMRM Analysis by GAA1 Repeat Length ≥ 675 (Yes, No) - FAS Population

Page: 6 of 6

GAA1 repeat length ≥ 675 : No

	Placebo (N=18)	Omaveloxolone 150 mg (N=10)
Week 36		
N	18	9
LS mean change from baseline	0.51	-1.62
SE	1.029	1.383
95% CI	(-1.55, 2.58)	(-4.39, 1.15)
LS mean difference (Omaveloxolone-Placebo)		-2.14
SE		1.683
95% CI		(-5.51, 1.24)
p-value		0.2097
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.49
95% CI		(-1.30, 0.32)
Week 48		
N	18	9
LS mean change from baseline	0.85	-1.00
SE	0.992	1.335
95% CI	(-1.14, 2.84)	(-3.68, 1.67)
LS mean difference (Omaveloxolone-Placebo)		-1.85
SE		1.620
95% CI		(-5.11, 1.40)
p-value		0.2576
Hedge's g standardized mean difference (Omaveloxolone-Placebo)		-0.44
95% CI		(-1.25, 0.37)

Note 1: LS Mean and Hedges' g are from the MMRM model for FAS population with three way interaction added (subgroup*treatment*time)

Note 2: This analysis is based on mFARS using the 93-point scale. The primary analyses are based on mFARS using the 99-point scale.

Source: biib141/valueaccess/amnog/t-mfars93-mmrm-gaa1.sas Data Tag: FINAL Run Date: 25JUN2024