Nirogacestat (Ogsiveo®)

SpringWorks Therapeutics Ireland Limited

Behandlung erwachsener Patienten mit fortschreitenden Desmoidtumoren, die eine systemische Behandlung erfordern

Anhang 4-G zu Modul 4A

MMRM Analysen und prädefinierte MCID

Stand: 15.10.2025

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1 MMRM Analysen

1.1 BPI-SF

1.1.1 Table MMRM BPI-SF

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	3.2		3.3	
SD	3.23		3.31	
Median	1.9		2.3	
Min, Max	0, 9		0, 9	
Effect over Study Duration				
n (%)		67 (95.7)		69 (95.8)
LS Mean [2]		-1.567		-0.258
LS SE [2]		0.2228		0.2292
95% CI [2]		-2.007, -1.127		-0.711, 0.194
LS Mean Diff. to Placebo [2]		-1.309		
LS SE Diff. to Placebo [2]		0.2993		
95% CI [2]		-1.900, -0.717		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.70 [-1.048, -0.355]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	61 (84.7)	61 (84.7)
Mean	1.8	-1.2	2.9	-0.4
SD	2.62	1.89	3.02	1.48
Median	0.1	-0.6	2.3	0.0
Min, Max	0, 9	-7, 1	0, 9	-5, 2
LS Mean [2]		-1.293		-0.436
LS SE [2]		0.2663		0.2638
95% CI [2]		-1.820, -0.766		-0.959, 0.086
LS Mean Diff. to Placebo [2]		-0.857		
LS SE Diff. to Placebo [2]		0.3579		
95% CI [2]		-1.566, -0.148		
One-sided p-value [2]		0.0092		
Hedge's G (95% CI)		-0.41 [-0.773, -0.055]		

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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 3				
n (%)	57 (81.4)	57 (81.4)	62 (86.1)	62 (86.1)
Mean	1.6	-1.8	3.1	-0.1
SD	2.59	2.42	2.90	2.22
Median	0.0	-0.9	2.8	0.0
Min, Max	0, 9	-8, 1	0, 8	-5, 7
LS Mean [2]		-1.584		-0.083
LS SE [2]		0.3257		0.3189
95% CI [2]		-2.228, -0.939		-0.714, 0.548
LS Mean Diff. to Placebo [2]		-1.501		
LS SE Diff. to Placebo [2]		0.4421		
95% CI [2]		-2.376, -0.625		
One-sided p-value [2]		0.0005		
Hedge's G (95% CI)		-0.60 [-0.971, -0.236]		

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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 4				
n (%)	43 (61.4)	43 (61.4)	43 (59.7)	43 (59.7)
Mean	1.1	-2.1	3.3	0.3
SD	2.17	2.89	3.00	2.17
Median	0.0	-1.0	3.1	0.0
Min, Max	0, 8	-9, 4	0, 9	-4, 8
LS Mean [2]		-1.809		0.075
LS SE [2]		0.3323		0.3273
95% CI [2]		-2.467, -1.151		-0.573, 0.724
LS Mean Diff. to Placebo [2]		-1.884		
LS SE Diff. to Placebo [2]		0.4528		
95% CI [2]		-2.781, -0.987		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.87 [-1.313, -0.429]		

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Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 5				
n (%)	44 (62.9)	44 (62.9)	46 (63.9)	45 (62.5)
Mean	1.3	-1.6	3.2	-0.2
SD	2.15	2.02	2.95	2.40
Median	0.0	-0.8	2.9	0.0
Min, Max	0, 8	-7, 1	0, 9	-6, 7
LS Mean [2]		-1.536		-0.064
LS SE [2]		0.2992		0.2939
95% CI [2]		-2.128, -0.943		-0.646, 0.517
LS Mean Diff. to Placebo [2]		-1.471		
LS SE Diff. to Placebo [2]		0.4046		
95% CI [2]		-2.273, -0.670		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-0.74 [-1.174, -0.314]		

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Pain at its Worst in Last 24 Hours				
Cycle 6				
n (%)	46 (65.7)	46 (65.7)	46 (63.9)	46 (63.9)
Mean	1.4	-1.3	2.9	-0.2
SD	2.53	2.71	2.97	2.10
Median	0.0	-0.6	2.6	0.0
Min, Max	0, 10	-9, 8	0, 10	-6, 5
LS Mean [2]		-1.511		-0.130
LS SE [2]		0.3127		0.3087
95% CI [2]		-2.130, -0.892		-0.741, 0.481
LS Mean Diff. to Placebo [2]		-1.381		
LS SE Diff. to Placebo [2]		0.4252		
95% CI [2]		-2.223, -0.539		
One-sided p-value [2]		0.0008		
Hedge's G (95% CI)		-0.66 [-1.075, -0.236]		

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Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 7				
n (%)	45 (64.3)	45 (64.3)	40 (55.6)	40 (55.6)
Mean	1.8	-1.3	3.1	-0.5
SD	2.40	2.42	3.20	2.42
Median	0.0	-0.6	2.4	0.0
Min, Max	0, 8	-8, 4	0, 9	-7, 5
LS Mean [2]		-1.137		-0.300
LS SE [2]		0.3000		0.3009
95% CI [2]		-1.730, -0.544		-0.895, 0.295
LS Mean Diff. to Placebo [2]		-0.837		
LS SE Diff. to Placebo [2]		0.4102		
95% CI [2]		-1.649, -0.025		
One-sided p-value [2]		0.0217		
Hedge's G (95% CI)		-0.43 [-0.857, 0.004]		

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Pain at its Worst in Last 24 Hours				
Cycle 8				
n (%)	39 (55.7)	39 (55.7)	35 (48.6)	35 (48.6)
Mean	1.9	-1.3	3.4	0.1
SD	2.83	2.47	3.30	2.49
Median	0.0	-0.8	3.5	0.0
Min, Max	0, 8	-8, 5	0, 10	-6, 6
LS Mean [2]		-1.223		0.114
LS SE [2]		0.3157		0.3184
95% CI [2]		-1.847, -0.598		-0.516, 0.744
LS Mean Diff. to Placebo [2]		-1.336		
LS SE Diff. to Placebo [2]		0.4345		
95% CI [2]		-2.196, -0.477		
One-sided p-value [2]		0.0013		
Hedge's G (95% CI)		-0.69 [-1.162, -0.223]		

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Intent-to-Treat Population

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Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 9				
n (%)	41 (58.6)	41 (58.6)	31 (43.1)	31 (43.1)
Mean	1.5	-1.7	3.6	-0.2
SD	2.48	2.28	3.33	2.48
Median	0.0	-1.0	3.0	0.0
Min, Max	0, 8	-9, 2	0, 10	-5, 6
LS Mean [2]		-1.542		0.000
LS SE [2]		0.2818		0.2912
95% CI [2]		-2.099, -0.985		-0.575, 0.576
LS Mean Diff. to Placebo [2]		-1.542		
LS SE Diff. to Placebo [2]		0.3892		
95% CI [2]		-2.312, -0.772		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.89 [-1.381, -0.404]		

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[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 10				
n (%)	40 (57.1)	40 (57.1)	31 (43.1)	31 (43.1)
Mean	1.3	-1.7	3.3	-0.1
SD	2.34	2.27	3.28	2.16
Median	0.0	-0.8	2.7	0.0
Min, Max	0, 8	-7, 3	0, 9	-5, 5
LS Mean [2]		-1.553		-0.045
LS SE [2]		0.2645		0.2732
95% CI [2]		-2.076, -1.030		-0.585, 0.495
LS Mean Diff. to Placebo [2]		-1.508		
LS SE Diff. to Placebo [2]		0.3630		
95% CI [2]		-2.226, -0.790		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.94 [-1.431, -0.444]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 11				
n (%)	37 (52.9)	37 (52.9)	28 (38.9)	28 (38.9)
Mean	1.2	-1.8	3.1	-0.2
SD	2.23	2.25	2.90	2.13
Median	0.0	-1.0	3.1	0.0
Min, Max	0, 8	-9, 0	0, 9	-5, 6
LS Mean [2]		-1.696		-0.238
LS SE [2]		0.2447		0.2565
95% CI [2]		-2.180, -1.212		-0.744, 0.269
LS Mean Diff. to Placebo [2]		-1.458		
LS SE Diff. to Placebo [2]		0.3356		
95% CI [2]		-2.122, -0.794		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.02 [-1.538, -0.496]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 12				
n (%)	40 (57.1)	40 (57.1)	26 (36.1)	26 (36.1)
Mean	1.7	-1.5	2.7	-0.8
SD	2.53	2.17	2.98	1.88
Median	0.0	-0.4	1.5	-0.2
Min, Max	0, 8	-7, 1	0, 9	-4, 3
LS Mean [2]		-1.278		-0.199
LS SE [2]		0.2528		0.2725
95% CI [2]		-1.778, -0.778		-0.737, 0.339
LS Mean Diff. to Placebo [2]		-1.078		
LS SE Diff. to Placebo [2]		0.3537		
95% CI [2]		-1.778, -0.379		
One-sided p-value [2]		0.0014		
Hedge's G (95% CI)		-0.71 [-1.218, -0.201]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	1.2	-1.9	2.8	-0.2
SD	2.34	2.44	3.03	2.34
Median	0.0	-0.9	1.8	0.0
Min, Max	0, 8	-9, 0	0, 9	-4, 7
LS Mean [2]		-1.511		-0.184
LS SE [2]		0.2796		0.3034
95% CI [2]		-2.065, -0.958		-0.783, 0.416
LS Mean Diff. to Placebo [2]		-1.328		
LS SE Diff. to Placebo [2]		0.3969		
95% CI [2]		-2.113, -0.542		
One-sided p-value [2]		0.0005		
Hedge's G (95% CI)		-0.84 [-1.389, -0.293]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 14				
n (%)	35 (50.0)	35 (50.0)	25 (34.7)	25 (34.7)
Mean	1.3	-1.6	3.0	-0.3
SD	2.32	2.10	3.28	2.37
Median	0.0	-1.0	1.6	0.0
Min, Max	0, 8	-7, 3	0, 10	-5, 7
LS Mean [2]		-1.555		-0.038
LS SE [2]		0.2664		0.2872
95% CI [2]		-2.081, -1.028		-0.605, 0.530
LS Mean Diff. to Placebo [2]		-1.517		
LS SE Diff. to Placebo [2]		0.3750		
95% CI [2]		-2.259, -0.775		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.00 [-1.542, -0.455]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 15				
n (%)	39 (55.7)	39 (55.7)	23 (31.9)	23 (31.9)
Mean	1.3	-1.8	3.0	-0.9
SD	2.40	2.39	3.18	2.69
Median	0.0	-0.9	2.7	0.0
Min, Max	0, 8	-9, 2	0, 9	-8, 3
LS Mean [2]		-1.582		-0.108
LS SE [2]		0.2675		0.2966
95% CI [2]		-2.111, -1.053		-0.694, 0.477
LS Mean Diff. to Placebo [2]		-1.474		
LS SE Diff. to Placebo [2]		0.3827		
95% CI [2]		-2.230, -0.718		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.93 [-1.471, -0.390]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 16				
n (%)	38 (54.3)	38 (54.3)	25 (34.7)	25 (34.7)
Mean	1.1	-1.9	2.9	-1.0
SD	2.19	2.46	3.31	2.85
Median	0.0	-0.8	1.0	0.0
Min, Max	0, 8	-9, 2	0, 9	-9, 4
LS Mean [2]		-1.672		-0.500
LS SE [2]		0.2620		0.2886
95% CI [2]		-2.190, -1.155		-1.069, 0.070
LS Mean Diff. to Placebo [2]		-1.172		
LS SE Diff. to Placebo [2]		0.3731		
95% CI [2]		-1.909, -0.435		
One-sided p-value [2]		0.0010		
Hedge's G (95% CI)		-0.76 [-1.278, -0.235]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 17				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	1.1	-1.9	3.0	0.2
SD	2.22	2.24	3.24	2.14
Median	0.0	-1.0	1.7	0.0
Min, Max	0, 9	-7, 1	0, 9	-7, 4
LS Mean [2]		-1.810		-0.400
LS SE [2]		0.2548		0.2845
95% CI [2]		-2.314, -1.306		-0.962, 0.162
LS Mean Diff. to Placebo [2]		-1.410		
LS SE Diff. to Placebo [2]		0.3643		
95% CI [2]		-2.130, -0.689		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.99 [-1.553, -0.420]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 18				
n (%)	32 (45.7)	32 (45.7)	21 (29.2)	21 (29.2)
Mean	1.0	-1.9	3.0	-0.2
SD	1.92	2.08	3.27	2.86
Median	0.0	-1.2	3.0	0.0
Min, Max	0, 7	-8, 0	0, 9	-7, 5
LS Mean [2]		-1.603		-0.128
LS SE [2]		0.2806		0.3152
95% CI [2]		-2.158, -1.048		-0.751, 0.495
LS Mean Diff. to Placebo [2]		-1.475		
LS SE Diff. to Placebo [2]		0.4061		
95% CI [2]		-2.279, -0.671		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-0.96 [-1.543, -0.382]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 19				
n (%)	32 (45.7)	32 (45.7)	23 (31.9)	23 (31.9)
Mean	1.1	-2.0	2.1	-0.5
SD	1.94	2.18	2.46	2.72
Median	0.0	-1.3	0.0	0.0
Min, Max	0, 7	-9, 1	0, 7	-6, 5
LS Mean [2]		-1.605		-0.651
LS SE [2]		0.2422		0.2727
95% CI [2]		-2.084, -1.126		-1.190, -0.112
LS Mean Diff. to Placebo [2]		-0.954		
LS SE Diff. to Placebo [2]		0.3468		
95% CI [2]		-1.640, -0.268		
One-sided p-value [2]		0.0034		
Hedge's G (95% CI)		-0.71 [-1.262, -0.158]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 20				
n (%)	33 (47.1)	33 (47.1)	17 (23.6)	17 (23.6)
Mean	1.2	-1.8	2.4	-1.0
SD	2.13	2.18	2.81	2.97
Median	0.0	-1.9	0.0	-0.5
Min, Max	0, 8	-9, 1	0, 8	-7, 6
LS Mean [2]		-1.611		-0.506
LS SE [2]		0.2576		0.3061
95% CI [2]		-2.121, -1.102		-1.111, 0.100
LS Mean Diff. to Placebo [2]		-1.106		
LS SE Diff. to Placebo [2]		0.3842		
95% CI [2]		-1.866, -0.345		
One-sided p-value [2]		0.0023		
Hedge's G (95% CI)		-0.78 [-1.389, -0.179]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 21				
n (%)	34 (48.6)	34 (48.6)	14 (19.4)	14 (19.4)
Mean	0.9	-2.0	2.6	-0.5
SD	1.85	2.51	2.86	2.76
Median	0.0	-1.0	1.9	-0.2
Min, Max	0, 8	-9, 1	0, 8	-6, 7
LS Mean [2]		-1.817		-0.633
LS SE [2]		0.2499		0.3066
95% CI [2]		-2.311, -1.322		-1.239, -0.027
LS Mean Diff. to Placebo [2]		-1.184		
LS SE Diff. to Placebo [2]		0.3797		
95% CI [2]		-1.935, -0.433		
One-sided p-value [2]		0.0011		
Hedge's G (95% CI)		-0.85 [-1.491, -0.201]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 22				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	0.6	-2.0	2.2	-1.1
SD	1.56	2.36	2.64	2.79
Median	0.0	-1.1	1.2	-0.2
Min, Max	0, 6	-9, 1	0, 8	-6, 6
LS Mean [2]		-1.871		-0.720
LS SE [2]		0.2471		0.2909
95% CI [2]		-2.359, -1.382		-1.295, -0.144
LS Mean Diff. to Placebo [2]		-1.151		
LS SE Diff. to Placebo [2]		0.3651		
95% CI [2]		-1.874, -0.428		
One-sided p-value [2]		0.0010		
Hedge's G (95% CI)		-0.85 [-1.443, -0.260]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	15 (20.8)	15 (20.8)
Mean	1.1	-1.6	1.8	0.1
SD	2.09	2.03	2.71	2.55
Median	0.0	-0.9	0.0	0.0
Min, Max	0, 8	-7, 2	0, 8	-6, 7
LS Mean [2]		-1.720		-0.243
LS SE [2]		0.2733		0.3350
95% CI [2]		-2.261, -1.178		-0.907, 0.420
LS Mean Diff. to Placebo [2]		-1.477		
LS SE Diff. to Placebo [2]		0.4154		
95% CI [2]		-2.300, -0.654		
One-sided p-value [2]		0.0003		
Hedge's G (95% CI)		-1.02 [-1.683, -0.365]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 24				
n (%)	23 (32.9)	23 (32.9)	12 (16.7)	12 (16.7)
Mean	1.2	-1.3	2.0	-0.7
SD	2.51	2.38	2.86	2.15
Median	0.0	-1.0	0.4	0.0
Min, Max	0, 8	-6, 5	0, 8	-6, 2
LS Mean [2]		-1.526		-0.528
LS SE [2]		0.3139		0.3868
95% CI [2]		-2.151, -0.902		-1.297, 0.241
LS Mean Diff. to Placebo [2]		-0.998		
LS SE Diff. to Placebo [2]		0.4842		
95% CI [2]		-1.962, -0.035		
One-sided p-value [2]		0.0212		
Hedge's G (95% CI)		-0.67 [-1.387, 0.044]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 25				
n (%)	20 (28.6)	20 (28.6)	6 (8.3)	6 (8.3)
Mean	0.5	-1.8	3.8	-0.9
SD	1.56	1.98	3.76	2.79
Median	0.0	-1.1	4.1	0.0
Min, Max	0, 6	-6, 0	0, 8	-6, 3
Cycle 26				
n (%)	13 (18.6)	13 (18.6)	4 (5.6)	4 (5.6)
Mean	1.4	-2.0	6.0	-0.2
SD	2.64	2.21	2.43	1.81
Median	0.0	-1.6	6.8	-0.5
Min, Max	0, 8	-6, 0	3, 8	-2, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 27				
n (%)	14 (20.0)	14 (20.0)	3 (4.2)	3 (4.2)
Mean	1.1	-1.7	6.7	1.2
SD	2.49	2.00	0.88	4.07
Median	0.0	-1.0	6.6	2.4
Min, Max	0, 8	-6, 0	6, 8	-3, 5
Cycle 28				
n (%)	16 (22.9)	16 (22.9)	3 (4.2)	3 (4.2)
Mean	1.1	-1.5	4.3	0.2
SD	2.29	1.97	3.93	4.45
Median	0.0	-1.0	5.0	0.0
Min, Max	0, 7	-5, 1	0, 8	-4, 5

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 29				
n (%)	13 (18.6)	13 (18.6)	3 (4.2)	3 (4.2)
Mean	1.2	-1.9	3.1	-1.1
SD	2.31	2.35	2.79	2.24
Median	0.0	-1.2	3.8	0.0
Min, Max	0, 6	-7, 2	0, 5	-4, 0
Cycle 30				
n (%)	11 (15.7)	11 (15.7)	5 (6.9)	5 (6.9)
Mean	0.7	-1.6	2.3	-2.9
SD	1.81	1.87	2.29	2.54
Median	0.0	-1.0	1.8	-3.3
Min, Max	0, 6	-5, 1	0, 6	-5, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 31				
n (%)	9 (12.9)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	0.9	-1.6	1.3	-4.3
SD	2.32	2.63	2.50	3.12
Median	0.0	-0.5	0.0	-5.1
Min, Max	0, 7	-7, 2	0, 5	-7, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	1.3	-0.8	4.0	2.5
SD	2.21	2.30	5.66	3.54
Median	0.0	-0.3	4.0	2.5
Min, Max	0, 5	-5, 2	0, 8	0, 5

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 33				
n (%)	6 (8.6)	6 (8.6)	0	0
Mean	1.2	-2.5		
SD	2.86	2.75		
Median	0.0	-1.5		
Min, Max	0, 7	-7, 0		
Cycle 34				
n (%)	4 (5.7)	4 (5.7)	0	0
Mean	1.8	-1.4		
SD	3.50	1.12		
Median	0.0	-1.3		
Min, Max	0, 7	-3, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.1		
SD	NA	NA		
Median	0.0	-2.1		
Min, Max	0, 0	-2, -2		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.1		
SD	NA	NA		
Median	0.0	-2.1		
Min, Max	0, 0	-2, -2		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain at its Worst in Last 24 Hours				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-7.0		
SD	NA	NA		
Median	0.0	-7.0		
Min, Max	0, 0	-7, -7		
Follow-Up				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	0.5	-1.7		
SD	0.80	2.78		
Median	0.0	-0.8		
Min, Max	0, 2	-7, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	2.2		2.5	
SD	2.45		2.70	
Median	1.2		1.9	
Min, Max	0, 8		0, 9	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain Severity Subscale				
Effect over Study Duration				
n (%)		67 (95.7)		69 (95.8)
LS Mean [2]		-1.088		-0.243
LS SE [2]		0.1724		0.1782
95% CI [2]		-1.429, -0.747		-0.595, 0.109
LS Mean Diff. to Placebo [2]		-0.845		
LS SE Diff. to Placebo [2]		0.2318		
95% CI [2]		-1.303, -0.387		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-0.58 [-0.927, -0.241]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Severity Subscale				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	61 (84.7)	61 (84.7)
Mean	1.3	-0.9	2.0	-0.5
SD	2.09	1.48	2.29	1.34
Median	0.1	-0.3	1.5	0.0
Min, Max	0, 8	-6, 1	0, 8	-5, 2
LS Mean [2]		-0.926		-0.419
LS SE [2]		0.2156		0.2131
95% CI [2]		-1.352, -0.499		-0.841, 0.003
LS Mean Diff. to Placebo [2]		-0.507		
LS SE Diff. to Placebo [2]		0.2905		
95% CI [2]		-1.082, 0.069		
One-sided p-value [2]		0.0419		
Hedge's G (95% CI)		-0.30 [-0.660, 0.054]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 3				
n (%)	57 (81.4)	57 (81.4)	62 (86.1)	62 (86.1)
Mean	1.1	-1.2	2.2	-0.2
SD	1.99	1.75	2.28	1.77
Median	0.0	-0.5	1.8	0.0
Min, Max	0, 8	-6, 1	0, 7	-5, 6
LS Mean [2]		-1.154		-0.140
LS SE [2]		0.2474		0.2423
95% CI [2]		-1.644, -0.665		-0.619, 0.340
LS Mean Diff. to Placebo [2]		-1.015		
LS SE Diff. to Placebo [2]		0.3353		
95% CI [2]		-1.679, -0.351		
One-sided p-value [2]		0.0015		
Hedge's G (95% CI)		-0.54 [-0.903, -0.171]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 4				
n (%)	43 (61.4)	43 (61.4)	43 (59.7)	43 (59.7)
Mean	0.8	-1.4	2.4	0.1
SD	1.84	2.13	2.33	1.64
Median	0.0	-0.5	1.9	0.0
Min, Max	0, 8	-8, 3	0, 8	-3, 4
LS Mean [2]		-1.337		0.059
LS SE [2]		0.2657		0.2613
95% CI [2]		-1.863, -0.811		-0.458, 0.577
LS Mean Diff. to Placebo [2]		-1.396		
LS SE Diff. to Placebo [2]		0.3621		
95% CI [2]		-2.114, -0.679		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.81 [-1.248, -0.368]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Severity Subscale				
Cycle 5				
n (%)	44 (62.9)	44 (62.9)	46 (63.9)	45 (62.5)
Mean	0.9	-1.2	2.4	-0.3
SD	1.67	1.58	2.32	1.84
Median	0.0	-0.4	2.1	0.0
Min, Max	0, 7	-6, 0	0, 7	-5, 4
LS Mean [2]		-1.154		-0.107
LS SE [2]		0.2241		0.2198
95% CI [2]		-1.597, -0.710		-0.542, 0.328
LS Mean Diff. to Placebo [2]		-1.047		
LS SE Diff. to Placebo [2]		0.3018		
95% CI [2]		-1.644, -0.449		
One-sided p-value [2]		0.0004		
Hedge's G (95% CI)		-0.71 [-1.135, -0.279]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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Table 64.3.1
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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Severity Subscale				
Cycle 6				
n (%)	46 (65.7)	46 (65.7)	46 (63.9)	46 (63.9)
Mean	1.0	-0.8	2.1	-0.3
SD	1.99	1.92	2.29	1.68
Median	0.0	-0.3	1.5	0.0
Min, Max	0, 8	-6, 6	0, 8	-5, 3
LS Mean [2]		-1.070		-0.150
LS SE [2]		0.2297		0.2266
95% CI [2]		-1.525, -0.616		-0.598, 0.298
LS Mean Diff. to Placebo [2]		-0.920		
LS SE Diff. to Placebo [2]		0.3107		
95% CI [2]		-1.535, -0.305		
One-sided p-value [2]		0.0018		
Hedge's G (95% CI)		-0.59 [-1.012, -0.177]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain Severity Subscale				
Cycle 7				
n (%)	45 (64.3)	45 (64.3)	40 (55.6)	40 (55.6)
Mean	1.3	-0.9	2.3	-0.5
SD	1.89	1.65	2.59	2.00
Median	0.0	-0.3	1.1	0.0
Min, Max	0, 7	-6, 2	0, 8	-5, 3
LS Mean [2]		-0.820		-0.259
LS SE [2]		0.2275		0.2279
95% CI [2]		-1.270, -0.371		-0.710, 0.191
LS Mean Diff. to Placebo [2]		-0.561		
LS SE Diff. to Placebo [2]		0.3102		
95% CI [2]		-1.175, 0.052		
One-sided p-value [2]		0.0364		
Hedge's G (95% CI)		-0.38 [-0.807, 0.052]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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Table 64.3.1
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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 8				
n (%)	39 (55.7)	39 (55.7)	35 (48.6)	35 (48.6)
Mean	1.5	-0.8	2.6	0.0
SD	2.24	1.73	2.66	2.12
Median	0.0	-0.4	2.1	0.0
Min, Max	0, 7	-6, 4	0, 9	-5, 5
LS Mean [2]		-0.794		0.040
LS SE [2]		0.2481		0.2505
95% CI [2]		-1.285, -0.303		-0.456, 0.535
LS Mean Diff. to Placebo [2]		-0.834		
LS SE Diff. to Placebo [2]		0.3418		
95% CI [2]		-1.510, -0.157		
One-sided p-value [2]		0.0081		
Hedge's G (95% CI)		-0.55 [-1.014, -0.084]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Severity Subscale				
Cycle 9				
n (%)	41 (58.6)	41 (58.6)	31 (43.1)	31 (43.1)
Mean	1.1	-1.1	2.7	-0.3
SD	1.98	1.60	2.69	2.02
Median	0.0	-0.3	2.3	0.0
Min, Max	0, 7	-6, 1	0, 9	-5, 4
LS Mean [2]		-1.011		-0.058
LS SE [2]		0.2204		0.2277
95% CI [2]		-1.447, -0.575		-0.508, 0.392
LS Mean Diff. to Placebo [2]		-0.954		
LS SE Diff. to Placebo [2]		0.3046		
95% CI [2]		-1.556, -0.351		
One-sided p-value [2]		0.0011		
Hedge's G (95% CI)		-0.71 [-1.186, -0.225]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 10				
n (%)	40 (57.1)	40 (57.1)	31 (43.1)	31 (43.1)
Mean	1.0	-1.2	2.4	-0.2
SD	1.87	1.64	2.59	1.59
Median	0.0	-0.3	1.9	0.0
Min, Max	0, 7	-6, 2	0, 8	-4, 3
LS Mean [2]		-1.046		-0.086
LS SE [2]		0.2036		0.2103
95% CI [2]		-1.449, -0.644		-0.502, 0.329
LS Mean Diff. to Placebo [2]		-0.960		
LS SE Diff. to Placebo [2]		0.2791		
95% CI [2]		-1.512, -0.408		
One-sided p-value [2]		0.0004		
Hedge's G (95% CI)		-0.78 [-1.261, -0.289]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Severity Subscale				
Cycle 11				
n (%)	37 (52.9)	37 (52.9)	28 (38.9)	28 (38.9)
Mean	1.0	-1.1	2.3	-0.2
SD	1.87	1.56	2.43	1.77
Median	0.0	-0.3	1.8	-0.1
Min, Max	0, 7	-6, 0	0, 8	-4, 5
LS Mean [2]		-1.094		-0.260
LS SE [2]		0.1882		0.1974
95% CI [2]		-1.466, -0.722		-0.650, 0.130
LS Mean Diff. to Placebo [2]		-0.834		
LS SE Diff. to Placebo [2]		0.2578		
95% CI [2]		-1.343, -0.324		
One-sided p-value [2]		0.0008		
Hedge's G (95% CI)		-0.76 [-1.264, -0.248]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 12				
n (%)	40 (57.1)	40 (57.1)	26 (36.1)	26 (36.1)
Mean	1.2	-1.0	2.0	-0.7
SD	2.00	1.58	2.34	1.69
Median	0.0	-0.2	1.0	-0.2
Min, Max	0, 7	-6, 1	0, 8	-4, 3
LS Mean [2]		-0.885		-0.218
LS SE [2]		0.1902		0.2055
95% CI [2]		-1.261, -0.509		-0.623, 0.188
LS Mean Diff. to Placebo [2]		-0.667		
LS SE Diff. to Placebo [2]		0.2655		
95% CI [2]		-1.192, -0.142		
One-sided p-value [2]		0.0066		
Hedge's G (95% CI)		-0.58 [-1.086, -0.079]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	1.0	-1.2	2.2	-0.2
SD	1.95	1.67	2.55	2.14
Median	0.0	-0.3	1.0	0.0
Min, Max	0, 7	-6, 0	0, 8	-4, 6
LS Mean [2]		-0.964		-0.168
LS SE [2]		0.2090		0.2273
95% CI [2]		-1.378, -0.551		-0.617, 0.281
LS Mean Diff. to Placebo [2]		-0.797		
LS SE Diff. to Placebo [2]		0.2960		
95% CI [2]		-1.382, -0.211		
One-sided p-value [2]		0.0040		
Hedge's G (95% CI)		-0.67 [-1.215, -0.134]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 14				
n (%)	35 (50.0)	35 (50.0)	25 (34.7)	25 (34.7)
Mean	1.0	-1.0	2.3	-0.3
SD	1.93	1.51	2.64	1.94
Median	0.0	-0.4	1.0	0.0
Min, Max	0, 7	-5, 2	0, 8	-4, 6
LS Mean [2]		-1.012		-0.137
LS SE [2]		0.2076		0.2249
95% CI [2]		-1.422, -0.601		-0.581, 0.307
LS Mean Diff. to Placebo [2]		-0.874		
LS SE Diff. to Placebo [2]		0.2932		
95% CI [2]		-1.454, -0.295		
One-sided p-value [2]		0.0017		
Hedge's G (95% CI)		-0.74 [-1.267, -0.207]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 15				
n (%)	39 (55.7)	39 (55.7)	23 (31.9)	23 (31.9)
Mean	1.0	-1.2	2.2	-0.9
SD	1.94	1.68	2.57	2.42
Median	0.0	-0.3	1.3	0.0
Min, Max	0, 7	-6, 1	0, 8	-8, 2
LS Mean [2]		-1.022		-0.220
LS SE [2]		0.2160		0.2408
95% CI [2]		-1.448, -0.595		-0.695, 0.256
LS Mean Diff. to Placebo [2]		-0.802		
LS SE Diff. to Placebo [2]		0.3113		
95% CI [2]		-1.417, -0.187		
One-sided p-value [2]		0.0055		
Hedge's G (95% CI)		-0.63 [-1.153, -0.099]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 16				
n (%)	38 (54.3)	38 (54.3)	25 (34.7)	25 (34.7)
Mean	0.9	-1.2	2.2	-0.8
SD	1.81	1.79	2.72	2.54
Median	0.0	-0.4	0.5	0.0
Min, Max	0, 7	-6, 1	0, 8	-9, 3
LS Mean [2]		-1.100		-0.392
LS SE [2]		0.2143		0.2377
95% CI [2]		-1.523, -0.677		-0.861, 0.077
LS Mean Diff. to Placebo [2]		-0.708		
LS SE Diff. to Placebo [2]		0.3080		
95% CI [2]		-1.316, -0.099		
One-sided p-value [2]		0.0114		
Hedge's G (95% CI)		-0.56 [-1.071, -0.043]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 17				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	0.8	-1.3	2.2	0.1
SD	1.77	1.63	2.61	1.82
Median	0.0	-0.5	0.9	0.0
Min, Max	0, 7	-6, 1	0, 8	-6, 4
LS Mean [2]		-1.245		-0.365
LS SE [2]		0.2033		0.2278
95% CI [2]		-1.646, -0.843		-0.815, 0.085
LS Mean Diff. to Placebo [2]		-0.880		
LS SE Diff. to Placebo [2]		0.2921		
95% CI [2]		-1.457, -0.302		
One-sided p-value [2]		0.0015		
Hedge's G (95% CI)		-0.77 [-1.326, -0.216]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 18				
n (%)	32 (45.7)	32 (45.7)	21 (29.2)	21 (29.2)
Mean	0.8	-1.2	2.3	-0.2
SD	1.52	1.64	2.70	2.45
Median	0.0	-0.6	1.5	0.0
Min, Max	0, 6	-6, 1	0, 8	-6, 4
LS Mean [2]		-1.090		-0.144
LS SE [2]		0.2175		0.2455
95% CI [2]		-1.520, -0.660		-0.629, 0.341
LS Mean Diff. to Placebo [2]		-0.946		
LS SE Diff. to Placebo [2]		0.3158		
95% CI [2]		-1.571, -0.322		
One-sided p-value [2]		0.0016		
Hedge's G (95% CI)		-0.79 [-1.366, -0.224]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Severity Subscale				
Cycle 19				
n (%)	32 (45.7)	32 (45.7)	23 (31.9)	23 (31.9)
Mean	0.7	-1.4	1.5	-0.5
SD	1.33	1.56	1.80	2.27
Median	0.0	-0.9	0.0	0.0
Min, Max	0, 5	-6, 1	0, 5	-5, 5
LS Mean [2]		-1.193		-0.497
LS SE [2]		0.1869		0.2116
95% CI [2]		-1.563, -0.823		-0.915, -0.079
LS Mean Diff. to Placebo [2]		-0.696		
LS SE Diff. to Placebo [2]		0.2681		
95% CI [2]		-1.227, -0.166		
One-sided p-value [2]		0.0053		
Hedge's G (95% CI)		-0.67 [-1.220, -0.119]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 20				
n (%)	33 (47.1)	33 (47.1)	17 (23.6)	17 (23.6)
Mean	0.9	-1.3	1.6	-0.9
SD	1.57	1.56	1.96	2.37
Median	0.0	-0.9	0.0	-0.4
Min, Max	0, 6	-6, 1	0, 5	-6, 5
LS Mean [2]		-1.139		-0.442
LS SE [2]		0.1965		0.2337
95% CI [2]		-1.528, -0.750		-0.904, 0.020
LS Mean Diff. to Placebo [2]		-0.697		
LS SE Diff. to Placebo [2]		0.2926		
95% CI [2]		-1.276, -0.117		
One-sided p-value [2]		0.0094		
Hedge's G (95% CI)		-0.65 [-1.246, -0.049]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain Severity Subscale				
Cycle 21				
n (%)	34 (48.6)	34 (48.6)	14 (19.4)	14 (19.4)
Mean	0.6	-1.4	1.8	-0.4
SD	1.50	1.84	2.16	2.37
Median	0.0	-0.4	1.2	0.0
Min, Max	0, 7	-6, 1	0, 6	-4, 6
LS Mean [2]		-1.307		-0.479
LS SE [2]		0.2065		0.2543
95% CI [2]		-1.716, -0.899		-0.982, 0.024
LS Mean Diff. to Placebo [2]		-0.828		
LS SE Diff. to Placebo [2]		0.3160		
95% CI [2]		-1.453, -0.203		
One-sided p-value [2]		0.0049		
Hedge's G (95% CI)		-0.72 [-1.354, -0.077]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 22				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	0.4	-1.4	1.6	-0.9
SD	1.18	1.65	2.02	2.45
Median	0.0	-0.7	0.7	-0.4
Min, Max	0, 5	-6, 0	0, 6	-5, 6
LS Mean [2]		-1.302		-0.500
LS SE [2]		0.2028		0.2408
95% CI [2]		-1.703, -0.901		-0.976, -0.023
LS Mean Diff. to Placebo [2]		-0.802		
LS SE Diff. to Placebo [2]		0.3028		
95% CI [2]		-1.402, -0.203		
One-sided p-value [2]		0.0046		
Hedge's G (95% CI)		-0.72 [-1.306, -0.137]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	15 (20.8)	15 (20.8)
Mean	0.8	-1.1	1.3	0.1
SD	1.62	1.55	2.04	2.15
Median	0.0	-0.3	0.0	0.0
Min, Max	0, 6	-6, 1	0, 7	-5, 6
LS Mean [2]		-1.249		-0.276
LS SE [2]		0.2112		0.2607
95% CI [2]		-1.668, -0.831		-0.793, 0.240
LS Mean Diff. to Placebo [2]		-0.973		
LS SE Diff. to Placebo [2]		0.3225		
95% CI [2]		-1.612, -0.334		
One-sided p-value [2]		0.0016		
Hedge's G (95% CI)		-0.87 [-1.521, -0.222]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Severity Subscale				
Cycle 24				
n (%)	23 (32.9)	23 (32.9)	12 (16.7)	12 (16.7)
Mean	1.0	-0.8	1.4	-0.7
SD	1.96	1.60	2.04	1.87
Median	0.0	-0.4	0.2	0.0
Min, Max	0, 6	-4, 4	0, 6	-5, 1
LS Mean [2]		-1.108		-0.375
LS SE [2]		0.2510		0.3109
95% CI [2]		-1.607, -0.608		-0.993, 0.244
LS Mean Diff. to Placebo [2]		-0.733		
LS SE Diff. to Placebo [2]		0.3892		
95% CI [2]		-1.508, 0.042		
One-sided p-value [2]		0.0318		
Hedge's G (95% CI)		-0.62 [-1.329, 0.097]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 25				
n (%)	20 (28.6)	20 (28.6)	6 (8.3)	6 (8.3)
Mean	0.4	-1.2	2.7	-1.1
SD	1.30	1.25	2.54	2.13
Median	0.0	-0.7	3.0	-0.5
Min, Max	0, 5	-4, 0	0, 5	-4, 2
Cycle 26				
n (%)	13 (18.6)	13 (18.6)	4 (5.6)	4 (5.6)
Mean	1.1	-1.2	4.1	-0.8
SD	2.15	1.40	2.02	1.64
Median	0.0	-0.7	4.8	-0.8
Min, Max	0, 6	-3, 0	1, 6	-3, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 27				
n (%)	14 (20.0)	14 (20.0)	3 (4.2)	3 (4.2)
Mean	0.9	-1.1	4.3	-0.1
SD	2.13	1.46	0.38	3.19
Median	0.0	-0.5	4.4	1.2
Min, Max	0, 7	-5, 1	4, 5	-4, 2
Cycle 28				
n (%)	16 (22.9)	16 (22.9)	3 (4.2)	3 (4.2)
Mean	0.9	-1.1	2.6	-0.7
SD	1.90	1.36	2.28	3.32
Median	0.0	-0.6	3.3	0.0
Min, Max	0, 6	-4, 1	0, 4	-4, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 29				
n (%)	13 (18.6)	13 (18.6)	3 (4.2)	3 (4.2)
Mean	0.9	-1.3	1.9	-1.4
SD	1.94	1.69	1.86	2.14
Median	0.0	-0.7	2.0	-0.4
Min, Max	0, 5	-6, 1	0, 4	-4, 0
Cycle 30				
n (%)	11 (15.7)	11 (15.7)	5 (6.9)	5 (6.9)
Mean	0.5	-1.0	1.4	-2.7
SD	1.46	1.15	1.56	2.12
Median	0.0	-1.0	0.9	-3.6
Min, Max	0, 5	-3, 1	0, 4	-5, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 31				
n (%)	9 (12.9)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	0.8	-1.1	0.8	-3.8
SD	2.07	1.92	1.54	2.54
Median	0.0	-0.3	0.0	-4.7
Min, Max	0, 6	-6, 1	0, 3	-6, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	1.0	-0.4	2.2	1.1
SD	1.89	1.24	3.05	1.52
Median	0.0	-0.2	2.2	1.1
Min, Max	0, 5	-2, 1	0, 4	0, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain Severity Subscale				
Cycle 33				
n (%)	6 (8.6)	6 (8.6)	0	0
Mean	1.0	-1.7		
SD	2.47	2.12		
Median	0.0	-1.0		
Min, Max	0, 6	-6, 0		
Cycle 34				
n (%)	4 (5.7)	4 (5.7)	0	0
Mean	1.6	-0.9		
SD	3.10	0.89		
Median	0.0	-0.9		
Min, Max	0, 6	-2, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-1.5		
SD	NA	NA		
Median	0.0	-1.5		
Min, Max	0, 0	-1, -1		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-1.5		
SD	NA	NA		
Median	0.0	-1.5		
Min, Max	0, 0	-1, -1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Severity Subscale				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-5.1		
SD	NA	NA		
Median	0.0	-5.1		
Min, Max	0, 0	-5, -5		
Follow-Up				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	0.3	-1.4		
SD	0.45	2.67		
Median	0.0	-0.1		
Min, Max	0, 1	-6, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	2.3		2.2	
SD	2.84		2.63	
Median	0.8		1.0	
Min, Max	0, 10		0, 9	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain Interference Subscale				
Effect over Study Duration				
n (%)		67 (95.7)		69 (95.8)
LS Mean [2]		-0.999		-0.243
LS SE [2]		0.1718		0.1779
95% CI [2]		-1.339, -0.660		-0.594, 0.108
LS Mean Diff. to Placebo [2]		-0.756		
LS SE Diff. to Placebo [2]		0.2320		
95% CI [2]		-1.215, -0.298		
One-sided p-value [2]		0.0007		
Hedge's G (95% CI)		-0.52 [-0.866, -0.182]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	61 (84.7)	61 (84.7)
Mean	1.3	-0.8	1.7	-0.5
SD	2.36	1.42	2.27	1.37
Median	0.0	-0.1	0.9	0.0
Min, Max	0, 10	-6, 1	0, 10	-5, 3
LS Mean [2]		-0.757		-0.435
LS SE [2]		0.2125		0.2101
95% CI [2]		-1.178, -0.337		-0.851, -0.019
LS Mean Diff. to Placebo [2]		-0.322		
LS SE Diff. to Placebo [2]		0.2865		
95% CI [2]		-0.890, 0.245		
One-sided p-value [2]		0.1315		
Hedge's G (95% CI)		-0.20 [-0.551, 0.161]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 3				
n (%)	57 (81.4)	57 (81.4)	62 (86.1)	62 (86.1)
Mean	1.4	-1.1	1.8	-0.3
SD	2.48	1.78	2.12	1.47
Median	0.0	-0.6	1.0	0.0
Min, Max	0, 9	-6, 2	0, 9	-5, 2
LS Mean [2]		-0.930		-0.306
LS SE [2]		0.2343		0.2296
95% CI [2]		-1.394, -0.467		-0.760, 0.149
LS Mean Diff. to Placebo [2]		-0.624		
LS SE Diff. to Placebo [2]		0.3171		
95% CI [2]		-1.252, 0.004		
One-sided p-value [2]		0.0256		
Hedge's G (95% CI)		-0.35 [-0.711, 0.013]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 4				
n (%)	43 (61.4)	43 (61.4)	43 (59.7)	43 (59.7)
Mean	0.7	-1.5	1.8	0.0
SD	1.92	2.12	2.02	1.61
Median	0.0	-0.3	1.3	0.0
Min, Max	0, 10	-8, 1	0, 8	-4, 4
LS Mean [2]		-1.168		-0.110
LS SE [2]		0.2523		0.2484
95% CI [2]		-1.667, -0.668		-0.602, 0.381
LS Mean Diff. to Placebo [2]		-1.058		
LS SE Diff. to Placebo [2]		0.3435		
95% CI [2]		-1.738, -0.377		
One-sided p-value [2]		0.0013		
Hedge's G (95% CI)		-0.64 [-1.078, -0.211]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 5				
n (%)	44 (62.9)	44 (62.9)	46 (63.9)	45 (62.5)
Mean	0.8	-1.2	2.0	-0.2
SD	1.84	1.74	2.31	1.69
Median	0.0	-0.4	1.0	0.0
Min, Max	0, 10	-6, 1	0, 10	-6, 4
LS Mean [2]		-1.033		-0.238
LS SE [2]		0.2219		0.2182
95% CI [2]		-1.472, -0.594		-0.670, 0.193
LS Mean Diff. to Placebo [2]		-0.795		
LS SE Diff. to Placebo [2]		0.2994		
95% CI [2]		-1.388, -0.202		
One-sided p-value [2]		0.0045		
Hedge's G (95% CI)		-0.54 [-0.965, -0.118]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 6				
n (%)	46 (65.7)	46 (65.7)	46 (63.9)	46 (63.9)
Mean	0.8	-1.0	1.7	-0.3
SD	1.82	1.84	2.20	1.47
Median	0.0	-0.2	0.8	0.0
Min, Max	0, 10	-5, 3	0, 10	-4, 3
LS Mean [2]		-1.083		-0.269
LS SE [2]		0.2044		0.2022
95% CI [2]		-1.487, -0.678		-0.669, 0.131
LS Mean Diff. to Placebo [2]		-0.814		
LS SE Diff. to Placebo [2]		0.2745		
95% CI [2]		-1.357, -0.271		
One-sided p-value [2]		0.0018		
Hedge's G (95% CI)		-0.59 [-1.008, -0.173]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 7				
n (%)	45 (64.3)	45 (64.3)	40 (55.6)	40 (55.6)
Mean	1.1	-0.9	1.9	-0.4
SD	2.15	1.84	2.48	1.83
Median	0.0	-0.2	0.5	0.0
Min, Max	0, 10	-5, 3	0, 10	-5, 3
LS Mean [2]		-0.761		-0.294
LS SE [2]		0.2252		0.2255
95% CI [2]		-1.206, -0.315		-0.739, 0.152
LS Mean Diff. to Placebo [2]		-0.467		
LS SE Diff. to Placebo [2]		0.3072		
95% CI [2]		-1.075, 0.141		
One-sided p-value [2]		0.0654		
Hedge's G (95% CI)		-0.32 [-0.746, 0.111]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 8				
n (%)	39 (55.7)	39 (55.7)	35 (48.6)	35 (48.6)
Mean	1.3	-1.1	2.3	0.0
SD	2.40	1.81	2.59	1.61
Median	0.0	-0.4	1.5	0.0
Min, Max	0, 10	-5, 2	0, 10	-4, 3
LS Mean [2]		-0.967		-0.079
LS SE [2]		0.2027		0.2032
95% CI [2]		-1.368, -0.567		-0.480, 0.323
LS Mean Diff. to Placebo [2]		-0.889		
LS SE Diff. to Placebo [2]		0.2744		
95% CI [2]		-1.431, -0.346		
One-sided p-value [2]		0.0008		
Hedge's G (95% CI)		-0.72 [-1.190, -0.248]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 9				
n (%)	41 (58.6)	41 (58.6)	31 (43.1)	31 (43.1)
Mean	1.2	-1.1	2.5	-0.1
SD	2.45	1.74	2.60	1.84
Median	0.0	-0.6	2.1	0.0
Min, Max	0, 10	-6, 1	0, 10	-5, 3
LS Mean [2]		-0.964		-0.197
LS SE [2]		0.2042		0.2097
95% CI [2]		-1.368, -0.561		-0.611, 0.217
LS Mean Diff. to Placebo [2]		-0.767		
LS SE Diff. to Placebo [2]		0.2799		
95% CI [2]		-1.321, -0.214		
One-sided p-value [2]		0.0034		
Hedge's G (95% CI)		-0.61 [-1.091, -0.137]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 10				
n (%)	40 (57.1)	40 (57.1)	31 (43.1)	31 (43.1)
Mean	1.0	-1.2	2.2	0.1
SD	2.16	1.74	2.64	1.73
Median	0.0	-0.6	1.1	0.0
Min, Max	0, 10	-5, 2	0, 10	-3, 5
LS Mean [2]		-0.950		-0.092
LS SE [2]		0.2020		0.2083
95% CI [2]		-1.349, -0.551		-0.504, 0.319
LS Mean Diff. to Placebo [2]		-0.857		
LS SE Diff. to Placebo [2]		0.2771		
95% CI [2]		-1.405, -0.310		
One-sided p-value [2]		0.0012		
Hedge's G (95% CI)		-0.70 [-1.181, -0.215]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 11				
n (%)	37 (52.9)	37 (52.9)	28 (38.9)	28 (38.9)
Mean	0.9	-1.1	1.9	0.0
SD	2.18	1.91	2.43	1.37
Median	0.0	-0.3	1.3	0.0
Min, Max	0, 10	-5, 3	0, 10	-3, 3
LS Mean [2]		-0.986		-0.246
LS SE [2]		0.1869		0.1957
95% CI [2]		-1.356, -0.617		-0.633, 0.140
LS Mean Diff. to Placebo [2]		-0.740		
LS SE Diff. to Placebo [2]		0.2564		
95% CI [2]		-1.247, -0.234		
One-sided p-value [2]		0.0022		
Hedge's G (95% CI)		-0.68 [-1.181, -0.172]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 12				
n (%)	40 (57.1)	40 (57.1)	26 (36.1)	26 (36.1)
Mean	1.3	-0.9	1.7	-0.5
SD	2.34	1.74	2.11	1.62
Median	0.0	-0.3	0.7	0.0
Min, Max	0, 10	-5, 3	0, 8	-4, 4
LS Mean [2]		-0.785		-0.250
LS SE [2]		0.1881		0.2024
95% CI [2]		-1.157, -0.414		-0.650, 0.149
LS Mean Diff. to Placebo [2]		-0.535		
LS SE Diff. to Placebo [2]		0.2623		
95% CI [2]		-1.053, -0.017		
One-sided p-value [2]		0.0216		
Hedge's G (95% CI)		-0.47 [-0.973, 0.027]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	1.1	-1.1	1.8	-0.2
SD	2.32	1.88	2.15	1.95
Median	0.0	-0.6	0.8	0.0
Min, Max	0, 9	-5, 4	0, 8	-4, 4
LS Mean [2]		-0.853		-0.209
LS SE [2]		0.2088		0.2264
95% CI [2]		-1.265, -0.440		-0.656, 0.238
LS Mean Diff. to Placebo [2]		-0.644		
LS SE Diff. to Placebo [2]		0.2959		
95% CI [2]		-1.229, -0.059		
One-sided p-value [2]		0.0156		
Hedge's G (95% CI)		-0.55 [-1.081, -0.011]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 14				
n (%)	35 (50.0)	35 (50.0)	25 (34.7)	25 (34.7)
Mean	1.1	-0.9	2.2	-0.1
SD	2.36	1.78	2.78	1.72
Median	0.0	-0.6	0.7	0.0
Min, Max	0, 9	-5, 4	0, 10	-3, 4
LS Mean [2]		-0.888		-0.070
LS SE [2]		0.2061		0.2227
95% CI [2]		-1.295, -0.481		-0.510, 0.369
LS Mean Diff. to Placebo [2]		-0.818		
LS SE Diff. to Placebo [2]		0.2908		
95% CI [2]		-1.393, -0.244		
One-sided p-value [2]		0.0028		
Hedge's G (95% CI)		-0.70 [-1.224, -0.167]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 15				
n (%)	39 (55.7)	39 (55.7)	23 (31.9)	23 (31.9)
Mean	1.2	-1.0	2.4	-0.3
SD	2.43	1.90	2.94	2.23
Median	0.0	-0.4	1.3	0.0
Min, Max	0, 9	-5, 4	0, 10	-8, 4
LS Mean [2]		-0.937		-0.039
LS SE [2]		0.2111		0.2333
95% CI [2]		-1.354, -0.520		-0.499, 0.421
LS Mean Diff. to Placebo [2]		-0.899		
LS SE Diff. to Placebo [2]		0.3022		
95% CI [2]		-1.495, -0.302		
One-sided p-value [2]		0.0017		
Hedge's G (95% CI)		-0.72 [-1.250, -0.189]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 16				
n (%)	38 (54.3)	38 (54.3)	25 (34.7)	25 (34.7)
Mean	0.9	-1.1	2.3	-0.4
SD	2.03	1.94	2.88	2.31
Median	0.0	-0.4	1.7	0.0
Min, Max	0, 8	-5, 3	0, 10	-9, 4
LS Mean [2]		-1.018		-0.261
LS SE [2]		0.2110		0.2331
95% CI [2]		-1.435, -0.601		-0.721, 0.199
LS Mean Diff. to Placebo [2]		-0.757		
LS SE Diff. to Placebo [2]		0.3021		
95% CI [2]		-1.354, -0.160		
One-sided p-value [2]		0.0066		
Hedge's G (95% CI)		-0.61 [-1.122, -0.090]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain Interference Subscale				
Cycle 17				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	0.9	-1.2	2.1	0.3
SD	1.99	1.96	2.82	1.49
Median	0.0	-0.6	0.8	0.1
Min, Max	0, 7	-5, 3	0, 10	-3, 4
LS Mean [2]		-1.170		-0.200
LS SE [2]		0.2122		0.2371
95% CI [2]		-1.589, -0.751		-0.668, 0.269
LS Mean Diff. to Placebo [2]		-0.970		
LS SE Diff. to Placebo [2]		0.3059		
95% CI [2]		-1.575, -0.366		
One-sided p-value [2]		0.0009		
Hedge's G (95% CI)		-0.82 [-1.372, -0.258]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 18				
n (%)	32 (45.7)	32 (45.7)	21 (29.2)	21 (29.2)
Mean	0.8	-1.3	2.5	0.3
SD	1.78	1.97	2.92	1.76
Median	0.0	-0.6	1.6	0.0
Min, Max	0, 6	-5, 3	0, 10	-3, 4
LS Mean [2]		-1.108		0.004
LS SE [2]		0.2084		0.2346
95% CI [2]		-1.520, -0.696		-0.459, 0.467
LS Mean Diff. to Placebo [2]		-1.112		
LS SE Diff. to Placebo [2]		0.3013		
95% CI [2]		-1.707, -0.516		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-0.98 [-1.557, -0.395]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 19				
n (%)	32 (45.7)	32 (45.7)	23 (31.9)	23 (31.9)
Mean	0.9	-1.3	1.4	-0.1
SD	1.76	2.00	1.72	1.40
Median	0.0	-0.7	0.6	0.0
Min, Max	0, 6	-5, 3	0, 6	-3, 4
LS Mean [2]		-1.062		-0.268
LS SE [2]		0.2070		0.2346
95% CI [2]		-1.472, -0.652		-0.732, 0.196
LS Mean Diff. to Placebo [2]		-0.794		
LS SE Diff. to Placebo [2]		0.3006		
95% CI [2]		-1.389, -0.198		
One-sided p-value [2]		0.0047		
Hedge's G (95% CI)		-0.69 [-1.240, -0.138]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 20				
n (%)	33 (47.1)	33 (47.1)	17 (23.6)	17 (23.6)
Mean	1.0	-1.2	1.5	-0.4
SD	1.89	1.90	1.78	1.32
Median	0.0	-0.6	0.6	0.0
Min, Max	0, 6	-6, 2	0, 5	-3, 1
LS Mean [2]		-0.827		-0.281
LS SE [2]		0.2613		0.3107
95% CI [2]		-1.346, -0.308		-0.898, 0.335
LS Mean Diff. to Placebo [2]		-0.546		
LS SE Diff. to Placebo [2]		0.3972		
95% CI [2]		-1.335, 0.244		
One-sided p-value [2]		0.0865		
Hedge's G (95% CI)		-0.38 [-0.971, 0.209]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 21				
n (%)	34 (48.6)	34 (48.6)	14 (19.4)	14 (19.4)
Mean	0.7	-1.3	1.6	-0.1
SD	1.67	2.09	1.60	1.40
Median	0.0	-0.6	1.3	0.0
Min, Max	0, 6	-5, 3	0, 4	-3, 3
LS Mean [2]		-1.233		-0.429
LS SE [2]		0.2165		0.2650
95% CI [2]		-1.662, -0.804		-0.953, 0.096
LS Mean Diff. to Placebo [2]		-0.804		
LS SE Diff. to Placebo [2]		0.3312		
95% CI [2]		-1.461, -0.148		
One-sided p-value [2]		0.0084		
Hedge's G (95% CI)		-0.66 [-1.300, -0.027]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 22				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	0.4	-1.4	1.4	-0.5
SD	1.34	1.80	1.57	1.41
Median	0.0	-0.7	0.7	0.0
Min, Max	0, 6	-5, 1	0, 5	-3, 2
LS Mean [2]		-1.238		-0.483
LS SE [2]		0.1953		0.2319
95% CI [2]		-1.625, -0.851		-0.942, -0.023
LS Mean Diff. to Placebo [2]		-0.756		
LS SE Diff. to Placebo [2]		0.2907		
95% CI [2]		-1.332, -0.179		
One-sided p-value [2]		0.0054		
Hedge's G (95% CI)		-0.71 [-1.289, -0.121]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	15 (20.8)	15 (20.8)
Mean	0.9	-1.0	1.0	0.1
SD	1.82	1.97	1.28	1.02
Median	0.0	-0.5	0.0	0.0
Min, Max	0, 6	-5, 3	0, 4	-2, 3
LS Mean [2]		-1.172		-0.341
LS SE [2]		0.2080		0.2551
95% CI [2]		-1.584, -0.759		-0.846, 0.165
LS Mean Diff. to Placebo [2]		-0.831		
LS SE Diff. to Placebo [2]		0.3169		
95% CI [2]		-1.459, -0.202		
One-sided p-value [2]		0.0050		
Hedge's G (95% CI)		-0.76 [-1.400, -0.114]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Interference Subscale				
Cycle 24				
n (%)	23 (32.9)	23 (32.9)	12 (16.7)	12 (16.7)
Mean	1.1	-0.9	1.3	-0.3
SD	2.19	2.24	1.74	1.15
Median	0.0	-0.7	0.6	0.0
Min, Max	0, 6	-5, 4	0, 5	-3, 1
LS Mean [2]		-1.097		-0.500
LS SE [2]		0.2323		0.2893
95% CI [2]		-1.558, -0.636		-1.075, 0.074
LS Mean Diff. to Placebo [2]		-0.597		
LS SE Diff. to Placebo [2]		0.3612		
95% CI [2]		-1.314, 0.121		
One-sided p-value [2]		0.0510		
Hedge's G (95% CI)		-0.54 [-1.250, 0.169]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 25				
n (%)	20 (28.6)	20 (28.6)	6 (8.3)	6 (8.3)
Mean	0.4	-1.4	2.4	-0.7
SD	1.34	1.77	2.57	1.07
Median	0.0	-0.7	1.9	-0.2
Min, Max	0, 6	-5, 0	0, 6	-2, 0
Cycle 26				
n (%)	13 (18.6)	13 (18.6)	4 (5.6)	4 (5.6)
Mean	1.0	-1.4	4.0	-0.3
SD	1.92	1.76	2.05	0.68
Median	0.0	-0.9	3.9	-0.1
Min, Max	0, 5	-5, 1	2, 7	-1, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 27				
n (%)	14 (20.0)	14 (20.0)	3 (4.2)	3 (4.2)
Mean	0.8	-1.2	3.5	-0.5
SD	1.87	1.61	2.04	1.95
Median	0.0	-0.8	4.3	0.5
Min, Max	0, 6	-5, 0	1, 5	-3, 1
Cycle 28				
n (%)	16 (22.9)	16 (22.9)	3 (4.2)	3 (4.2)
Mean	0.8	-1.2	2.1	-0.7
SD	1.72	1.63	2.73	1.68
Median	0.0	-0.8	1.1	0.0
Min, Max	0, 6	-5, 1	0, 5	-3, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 29				
n (%)	13 (18.6)	13 (18.6)	3 (4.2)	3 (4.2)
Mean	1.0	-1.4	2.4	-0.9
SD	1.92	1.94	2.56	1.54
Median	0.0	-0.9	2.0	0.0
Min, Max	0, 6	-5, 2	0, 5	-3, 0
Cycle 30				
n (%)	11 (15.7)	11 (15.7)	5 (6.9)	5 (6.9)
Mean	0.4	-1.3	1.7	-1.7
SD	1.05	1.86	2.14	1.53
Median	0.0	-0.7	0.8	-2.5
Min, Max	0, 3	-5, 1	0, 5	-3, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 31				
n (%)	9 (12.9)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	0.8	-1.4	1.2	-2.5
SD	1.69	2.29	2.47	1.70
Median	0.0	-0.6	0.0	-3.0
Min, Max	0, 5	-5, 2	0, 5	-4, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	1.2	-0.7	0.6	0.3
SD	1.89	3.00	0.81	0.45
Median	0.0	-0.3	0.6	0.3
Min, Max	0, 4	-5, 4	0, 1	0, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Interference Subscale				
Cycle 33				
n (%)	6 (8.6)	6 (8.6)	0	0
Mean	0.8	-2.3		
SD	1.98	2.15		
Median	0.0	-1.9		
Min, Max	0, 5	-5, 0		
Cycle 34				
n (%)	4 (5.7)	4 (5.7)	0	0
Mean	1.2	-1.4		
SD	2.47	1.02		
Median	0.0	-1.0		
Min, Max	0, 5	-3, -1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
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Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain Interference Subscale				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-1.2		
SD	NA	NA		
Median	0.0	-1.2		
Min, Max	0, 0	-1, -1		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-1.2		
SD	NA	NA		
Median	0.0	-1.2		
Min, Max	0, 0	-1, -1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.3.1
Summary and Change from Baseline in BPI-SF Scores by Visit - Double-Blind Phase
API, Pain Severity Subscale, Pain Interference Subscale
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain Interference Subscale				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-4.3		
SD	NA	NA		
Median	0.0	-4.3		
Min, Max	0, 0	-4, -4		
Follow-Up				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	0.2	-1.3		
SD	0.32	2.51		
Median	0.0	-0.3		
Min, Max	0, 1	-6, 0		

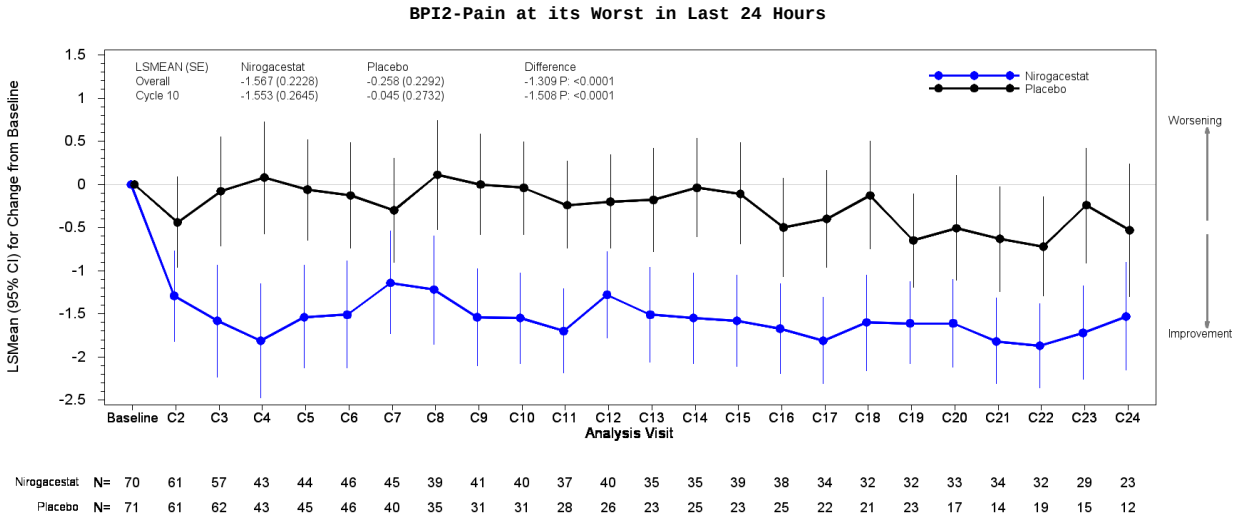
Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
API=Average Pain Intensity; BPI-SF=Brief Pain Inventory Short Form; CI = Confidence interval; LS=Least squares; SE=Standard error
Note: API was the (up to) 7-day average of BPI Question #3 - Worst Pain in Last 24 hours.
Note: A positive change from Baseline value indicated worsening of BPI and a negative change from Baseline value indicated improvement of BPI. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline BPI-SF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

1.1.2 Figure MMRM BPI-SF

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NIR-DT-301
2025_GBA

Figure 64.3.2
Mixed Model Repeated Measures: Change from Baseline in BPI-API SF Scores by Visit - Double Blind Phase
Intent-to-Treat Population

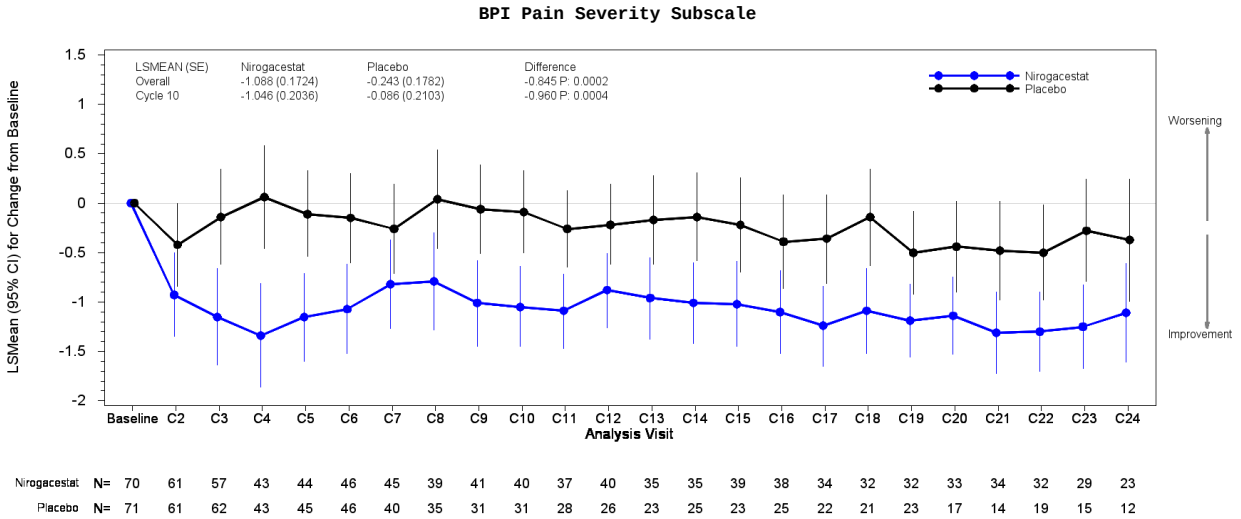


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.3.1, Dataset(s): ADSL, ADQS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

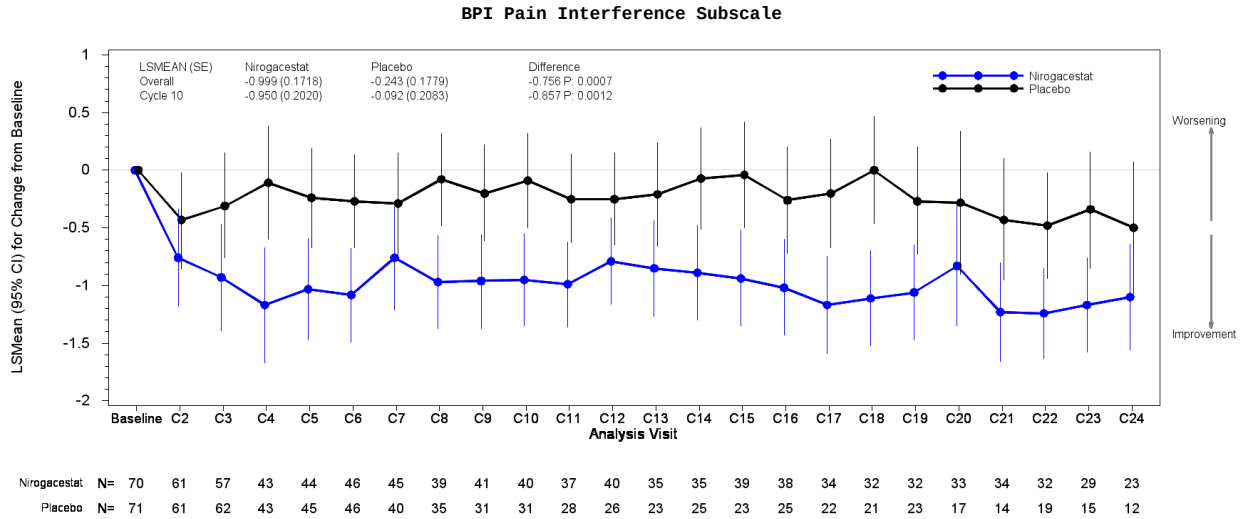
Figure 64.3.2
Mixed Model Repeated Measures: Change from Baseline in BPI-API SF Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.3.1, Dataset(s): ADSL, ADQS

Figure 64.3.2
Mixed Model Repeated Measures: Change from Baseline in BPI-API SF Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.3.1, Dataset(s): ADSL, ADQS

1.2 EORTC QLQ-C30

1.2.1 Table MMRM EORTC QLQ-C30

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Global Health Score/Quality of Life				
Baseline [1]				
n (%)	70 (100.0)		69 (95.8)	
Mean	59.9		63.3	
SD	24.38		20.68	
Median	58.3		66.7	
Min, Max	0, 100		17, 100	
Effect over Study Duration				
n (%)		68 (97.1)		66 (91.7)
LS Mean [2]		1.990		-2.261
LS SE [2]		1.6604		1.7816
95% CI [2]		-1.295, 5.274		-5.780, 1.259
LS Mean Diff. to Placebo [2]		4.250		
LS SE Diff. to Placebo [2]		2.2902		
95% CI [2]		-0.277, 8.778		
One-sided p-value [2]		0.0328		

Hedge's G (95% CI)	0.30 [-0.039, 0.642]

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	52 (72.2)	51 (70.8)
Mean	59.7	-1.3	63.0	0.2
SD	22.30	16.08	22.83	13.79
Median	62.5	0.0	66.7	0.0
Min, Max	0, 100	-42, 50	8, 100	-33, 33
LS Mean [2]		-1.884		-0.347
LS SE [2]		2.2670		2.3898
95% CI [2]		-6.381, 2.612		-5.088, 4.393
LS Mean Diff. to Placebo [2]		-1.537		
LS SE Diff. to Placebo [2]		3.1853		
95% CI [2]		-7.860, 4.786		
One-sided p-value [2]		0.6847		
Hedge's G (95% CI)		-0.09 [-0.462, 0.285]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	61.0	1.3	62.7	-1.1
SD	24.67	22.55	20.14	18.73
Median	58.3	0.0	66.7	0.0
Min, Max	0, 100	-92, 42	17, 100	-50, 58
LS Mean [2]		0.120		-0.660
LS SE [2]		2.7221		2.6321
95% CI [2]		-5.269, 5.510		-5.874, 4.554
LS Mean Diff. to Placebo [2]		0.780		
LS SE Diff. to Placebo [2]		3.6947		
95% CI [2]		-6.542, 8.102		
One-sided p-value [2]		0.4166		
Hedge's G (95% CI)		0.04 [-0.332, 0.410]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 4				
n (%)	45 (64.3)	45 (64.3)	37 (51.4)	35 (48.6)
Mean	64.6	-0.2	64.2	3.3
SD	21.48	21.72	18.41	18.10
Median	66.7	0.0	66.7	0.0
Min, Max	33, 100	-67, 42	25, 100	-25, 67
LS Mean [2]		-2.042		3.581
LS SE [2]		2.6797		2.9015
95% CI [2]		-7.364, 3.280		-2.183, 9.345
LS Mean Diff. to Placebo [2]		-5.623		
LS SE Diff. to Placebo [2]		3.8606		
95% CI [2]		-13.297, 2.051		
One-sided p-value [2]		0.9256		
Hedge's G (95% CI)		-0.32 [-0.763, 0.125]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 5				
n (%)	42 (60.0)	42 (60.0)	41 (56.9)	40 (55.6)
Mean	64.7	2.8	65.9	1.0
SD	19.72	20.71	17.06	15.12
Median	66.7	0.0	66.7	0.0
Min, Max	17, 100	-58, 50	33, 100	-33, 33
LS Mean [2]		1.655		2.921
LS SE [2]		2.2130		2.2541
95% CI [2]		-2.732, 6.042		-1.548, 7.390
LS Mean Diff. to Placebo [2]		-1.267		
LS SE Diff. to Placebo [2]		3.0480		
95% CI [2]		-7.314, 4.781		
One-sided p-value [2]		0.6607		
Hedge's G (95% CI)		-0.09 [-0.522, 0.345]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	60.3	-2.0	65.7	-1.2
SD	21.17	18.53	16.99	16.06
Median	66.7	0.0	62.5	0.0
Min, Max	8, 100	-50, 50	33, 100	-33, 33
LS Mean [2]		-2.900		0.362
LS SE [2]		2.5247		2.6257
95% CI [2]		-7.919, 2.119		-4.855, 5.580
LS Mean Diff. to Placebo [2]		-3.263		
LS SE Diff. to Placebo [2]		3.5447		
95% CI [2]		-10.314, 3.789		
One-sided p-value [2]		0.8200		
Hedge's G (95% CI)		-0.21 [-0.670, 0.251]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	62.6	1.6	63.5	-1.4
SD	23.24	19.86	19.87	22.05
Median	66.7	0.0	66.7	0.0
Min, Max	0, 100	-42, 42	17, 100	-67, 42
LS Mean [2]		-0.450		-0.431
LS SE [2]		2.7749		2.9555
95% CI [2]		-5.956, 5.056		-6.295, 5.433
LS Mean Diff. to Placebo [2]		-0.019		
LS SE Diff. to Placebo [2]		3.9664		
95% CI [2]		-7.895, 7.858		
One-sided p-value [2]		0.5019		
Hedge's G (95% CI)		-0.00 [-0.444, 0.442]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 8				
n (%)	42 (60.0)	42 (60.0)	30 (41.7)	29 (40.3)
Mean	63.5	4.2	61.1	-3.4
SD	22.08	16.69	19.74	18.57
Median	66.7	0.0	66.7	0.0
Min, Max	0, 100	-42, 42	17, 92	-50, 33
LS Mean [2]		2.961		-1.309
LS SE [2]		2.3052		2.6042
95% CI [2]		-1.616, 7.538		-6.479, 3.861
LS Mean Diff. to Placebo [2]		4.270		
LS SE Diff. to Placebo [2]		3.3859		
95% CI [2]		-2.457, 10.997		
One-sided p-value [2]		0.1053		
Hedge's G (95% CI)		0.29 [-0.183, 0.769]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	34 (47.2)	32 (44.4)
Mean	67.8	6.4	58.8	-3.1
SD	20.14	22.00	22.28	20.49
Median	66.7	8.3	66.7	-8.3
Min, Max	25, 100	-58, 58	8, 100	-58, 50
LS Mean [2]		3.237		-3.058
LS SE [2]		2.6556		2.9599
95% CI [2]		-2.032, 8.507		-8.930, 2.813
LS Mean Diff. to Placebo [2]		6.295		
LS SE Diff. to Placebo [2]		3.8811		
95% CI [2]		-1.411, 14.002		
One-sided p-value [2]		0.0541		
Hedge's G (95% CI)		0.36 [-0.094, 0.824]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	27 (37.5)
Mean	68.4	7.0	55.1	-7.1
SD	19.20	22.64	22.03	22.37
Median	66.7	4.2	58.3	0.0
Min, Max	33, 100	-58, 67	8, 92	-67, 42
LS Mean [2]		4.389		-5.962
LS SE [2]		2.7996		3.1696
95% CI [2]		-1.174, 9.952		-12.259, 0.336
LS Mean Diff. to Placebo [2]		10.350		
LS SE Diff. to Placebo [2]		4.1403		
95% CI [2]		2.117, 18.584		
One-sided p-value [2]		0.0072		
Hedge's G (95% CI)		0.61 [0.107, 1.115]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 11				
n (%)	33 (47.1)	33 (47.1)	26 (36.1)	26 (36.1)
Mean	66.2	3.0	61.2	-5.4
SD	25.60	28.48	20.81	22.72
Median	66.7	8.3	58.3	0.0
Min, Max	0, 100	-83, 50	0, 92	-83, 33
LS Mean [2]		1.012		0.586
LS SE [2]		3.4651		3.8274
95% CI [2]		-5.883, 7.906		-7.026, 8.199
LS Mean Diff. to Placebo [2]		0.425		
LS SE Diff. to Placebo [2]		5.0886		
95% CI [2]		-9.705, 10.555		
One-sided p-value [2]		0.4668		
Hedge's G (95% CI)		0.02 [-0.492, 0.536]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	23 (31.9)
Mean	64.4	3.0	64.6	-3.6
SD	22.17	21.02	17.59	23.55
Median	66.7	0.0	66.7	0.0
Min, Max	17, 100	-50, 50	17, 92	-67, 33
LS Mean [2]		-0.227		0.269
LS SE [2]		2.8193		3.2608
95% CI [2]		-5.834, 5.380		-6.213, 6.752
LS Mean Diff. to Placebo [2]		-0.497		
LS SE Diff. to Placebo [2]		4.2365		
95% CI [2]		-8.928, 7.934		
One-sided p-value [2]		0.5465		
Hedge's G (95% CI)		-0.03 [-0.564, 0.501]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	21 (29.2)
Mean	65.9	5.6	58.7	-6.3
SD	23.33	17.64	19.86	18.80
Median	66.7	0.0	58.3	-8.3
Min, Max	0, 100	-25, 50	25, 92	-50, 25
LS Mean [2]		4.024		-4.303
LS SE [2]		2.4258		2.9005
95% CI [2]		-0.803, 8.852		-10.071, 1.464
LS Mean Diff. to Placebo [2]		8.327		
LS SE Diff. to Placebo [2]		3.6912		
95% CI [2]		0.977, 15.678		
One-sided p-value [2]		0.0135		
Hedge's G (95% CI)		0.61 [0.049, 1.167]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	20 (27.8)
Mean	70.2	5.8	57.2	-6.3
SD	21.35	20.57	19.12	15.50
Median	75.0	0.0	54.2	0.0
Min, Max	17, 100	-25, 58	17, 92	-42, 17
LS Mean [2]		4.635		-5.363
LS SE [2]		2.4655		2.9726
95% CI [2]		-0.269, 9.538		-11.275, 0.549
LS Mean Diff. to Placebo [2]		9.998		
LS SE Diff. to Placebo [2]		3.7709		
95% CI [2]		2.491, 17.504		
One-sided p-value [2]		0.0048		
Hedge's G (95% CI)		0.72 [0.150, 1.294]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	64.8	3.5	60.9	-1.1
SD	18.35	19.46	19.21	18.24
Median	66.7	8.3	58.3	0.0
Min, Max	33, 100	-58, 50	17, 92	-50, 25
LS Mean [2]		2.443		-1.203
LS SE [2]		2.5251		2.9054
95% CI [2]		-2.585, 7.472		-6.987, 4.581
LS Mean Diff. to Placebo [2]		3.646		
LS SE Diff. to Placebo [2]		3.7538		
95% CI [2]		-3.837, 11.130		
One-sided p-value [2]		0.1673		
Hedge's G (95% CI)		0.26 [-0.286, 0.811]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	19 (26.4)
Mean	67.4	4.9	61.3	-5.3
SD	18.62	18.25	23.30	20.07
Median	66.7	0.0	66.7	0.0
Min, Max	33, 100	-25, 42	17, 92	-67, 25
LS Mean [2]		2.943		-3.090
LS SE [2]		2.4639		3.0882
95% CI [2]		-1.958, 7.845		-9.232, 3.052
LS Mean Diff. to Placebo [2]		6.033		
LS SE Diff. to Placebo [2]		3.8678		
95% CI [2]		-1.666, 13.732		
One-sided p-value [2]		0.0614		
Hedge's G (95% CI)		0.43 [-0.138, 0.997]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 17				
n (%)	31 (44.3)	31 (44.3)	18 (25.0)	17 (23.6)
Mean	68.3	8.6	57.4	-13.7
SD	19.77	19.30	24.23	26.34
Median	66.7	8.3	66.7	-8.3
Min, Max	17, 100	-33, 58	8, 92	-75, 25
LS Mean [2]		4.118		-10.799
LS SE [2]		2.7828		3.5644
95% CI [2]		-1.423, 9.659		-17.896, -3.701
LS Mean Diff. to Placebo [2]		14.917		
LS SE Diff. to Placebo [2]		4.4796		
95% CI [2]		5.992, 23.842		
One-sided p-value [2]		0.0007		
Hedge's G (95% CI)		0.96 [0.342, 1.586]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	65.7	4.8	58.8	-9.2
SD	19.29	19.21	27.90	23.06
Median	66.7	0.0	58.3	-8.3
Min, Max	25, 100	-33, 50	0, 100	-83, 25
LS Mean [2]		2.063		-6.286
LS SE [2]		2.8282		3.5626
95% CI [2]		-3.566, 7.693		-13.374, 0.803
LS Mean Diff. to Placebo [2]		8.349		
LS SE Diff. to Placebo [2]		4.4871		
95% CI [2]		-0.587, 17.285		
One-sided p-value [2]		0.0333		
Hedge's G (95% CI)		0.52 [-0.051, 1.095]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	16 (22.2)
Mean	62.9	2.8	63.0	-7.8
SD	22.25	23.45	21.05	18.38
Median	66.7	0.0	62.5	-4.2
Min, Max	0, 100	-58, 50	25, 100	-50, 25
LS Mean [2]		-0.366		-8.012
LS SE [2]		3.0930		4.2104
95% CI [2]		-6.542, 5.809		-16.417, 0.393
LS Mean Diff. to Placebo [2]		7.646		
LS SE Diff. to Placebo [2]		5.1974		
95% CI [2]		-2.736, 18.028		
One-sided p-value [2]		0.0731		
Hedge's G (95% CI)		0.43 [-0.173, 1.034]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	15 (20.8)
Mean	61.9	1.9	69.3	1.7
SD	20.72	22.71	19.42	11.44
Median	66.7	0.0	66.7	0.0
Min, Max	8, 100	-58, 50	33, 100	-17, 25
LS Mean [2]		0.137		1.638
LS SE [2]		3.0496		4.0921
95% CI [2]		-5.968, 6.243		-6.559, 9.835
LS Mean Diff. to Placebo [2]		-1.500		
LS SE Diff. to Placebo [2]		5.0575		
95% CI [2]		-11.638, 8.638		
One-sided p-value [2]		0.6161		
Hedge's G (95% CI)		-0.09 [-0.710, 0.530]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	13 (18.1)
Mean	66.4	8.3	66.1	-1.9
SD	18.63	18.69	23.90	21.29
Median	66.7	8.3	66.7	0.0
Min, Max	33, 100	-33, 50	17, 92	-42, 42
LS Mean [2]		3.458		-3.043
LS SE [2]		2.5192		3.5624
95% CI [2]		-1.561, 8.477		-10.141, 4.055
LS Mean Diff. to Placebo [2]		6.501		
LS SE Diff. to Placebo [2]		4.3175		
95% CI [2]		-2.109, 15.111		
One-sided p-value [2]		0.0683		
Hedge's G (95% CI)		0.46 [-0.191, 1.112]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	18 (25.0)
Mean	69.4	10.8	68.0	0.5
SD	17.13	20.88	18.27	14.98
Median	66.7	8.3	66.7	0.0
Min, Max	25, 100	-25, 50	17, 100	-25, 33
LS Mean [2]		5.992		1.859
LS SE [2]		2.2727		2.8688
95% CI [2]		1.467, 10.517		-3.852, 7.570
LS Mean Diff. to Placebo [2]		4.134		
LS SE Diff. to Placebo [2]		3.6021		
95% CI [2]		-3.043, 11.311		
One-sided p-value [2]		0.1274		
Hedge's G (95% CI)		0.33 [-0.259, 0.910]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	65.8	9.2	60.3	-7.1
SD	21.29	18.14	18.05	14.37
Median	66.7	8.3	66.7	-8.3
Min, Max	17, 100	-25, 50	17, 83	-25, 25
LS Mean [2]		7.291		-6.829
LS SE [2]		2.4482		3.3676
95% CI [2]		2.404, 12.178		-13.556, -0.102
LS Mean Diff. to Placebo [2]		14.120		
LS SE Diff. to Placebo [2]		4.1292		
95% CI [2]		5.867, 22.374		
One-sided p-value [2]		0.0006		
Hedge's G (95% CI)		1.08 [0.382, 1.769]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	10 (13.9)
Mean	66.7	9.1	62.9	-6.7
SD	21.25	22.65	19.85	9.46
Median	66.7	0.0	66.7	-8.3
Min, Max	33, 100	-25, 58	17, 92	-25, 8
LS Mean [2]		3.149		-2.518
LS SE [2]		3.4195		4.6837
95% CI [2]		-3.747, 10.045		-11.971, 6.934
LS Mean Diff. to Placebo [2]		5.667		
LS SE Diff. to Placebo [2]		5.8071		
95% CI [2]		-6.058, 17.393		
One-sided p-value [2]		0.1674		
Hedge's G (95% CI)		0.36 [-0.400, 1.117]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Global Health Score/Quality of Life				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	68.9	9.6	41.7	-16.7
SD	20.38	22.61	18.63	11.79
Median	66.7	0.0	41.7	-8.3
Min, Max	33, 100	-25, 50	17, 67	-33, -8
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	66.7	5.3	44.4	-19.4
SD	23.27	17.19	16.39	6.80
Median	66.7	8.3	45.8	-20.8
Min, Max	33, 100	-25, 25	17, 67	-25, -8

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Global Health Score/Quality of Life				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	63.2	12.5	56.3	-10.4
SD	15.67	21.47	24.88	26.68
Median	58.3	16.7	58.3	0.0
Min, Max	42, 92	-33, 42	25, 83	-50, 8
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	63.2	5.6	58.3	-8.3
SD	18.28	22.00	35.36	11.79
Median	66.7	4.2	58.3	-8.3
Min, Max	33, 100	-25, 50	33, 83	-17, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Global Health Score/Quality of Life				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	61.4	3.8	44.4	-19.4
SD	18.74	14.61	9.62	12.73
Median	58.3	8.3	50.0	-16.7
Min, Max	33, 100	-25, 25	33, 50	-33, -8
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	57.3	14.6	52.1	-2.1
SD	11.30	20.77	4.17	7.98
Median	54.2	8.3	50.0	-4.2
Min, Max	42, 75	-8, 50	50, 58	-8, 8

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Global Health Score/Quality of Life				
Cycle 31				
n (%)	6 (8.6)	6 (8.6)	4 (5.6)	4 (5.6)
Mean	65.3	4.2	62.5	-8.3
SD	18.57	21.57	14.43	15.21
Median	62.5	0.0	58.3	-8.3
Min, Max	50, 100	-25, 42	50, 83	-25, 8
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	56.9	5.6	79.2	-4.2
SD	9.74	18.00	5.89	5.89
Median	54.2	4.2	79.2	-4.2
Min, Max	50, 75	-17, 33	75, 83	-8, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Global Health Score/Quality of Life				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	65.0	5.0		
SD	14.91	13.94		
Median	66.7	8.3		
Min, Max	50, 83	-8, 25		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	66.7	-16.7		
SD	NA	NA		
Median	66.7	-16.7		
Min, Max	67, 67	-17, -17		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Global Health Score/Quality of Life				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	50.0	0.0		
SD	NA	NA		
Median	50.0	0.0		
Min, Max	50, 50	0, 0		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	50.0	0.0		
SD	NA	NA		
Median	50.0	0.0		
Min, Max	50, 50	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Global Health Score/Quality of Life				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	50.0	8.3		
SD	NA	NA		
Median	50.0	8.3		
Min, Max	50, 50	8, 8		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	58.3	-6.0	50.0	8.3
SD	23.57	30.32	NA	NA
Median	66.7	-8.3	50.0	8.3
Min, Max	17, 83	-50, 50	50, 50	8, 8

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	77.5		77.1	
SD	22.23		21.97	
Median	80.0		80.0	
Min, Max	7, 100		13, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		7.322		-0.774
LS SE [2]		1.0155		1.1437
95% CI [2]		5.317, 9.328		-3.031, 1.482
LS Mean Diff. to Placebo [2]		8.096		
LS SE Diff. to Placebo [2]		1.4345		
95% CI [2]		5.264, 10.929		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.91 [0.557, 1.266]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	79.3	2.5	80.4	1.1
SD	21.97	12.60	17.45	9.34
Median	86.7	0.0	80.0	0.0
Min, Max	7, 100	-20, 47	33, 100	-20, 33
LS Mean [2]		2.536		1.066
LS SE [2]		1.5569		1.6049
95% CI [2]		-0.543, 5.616		-2.108, 4.240
LS Mean Diff. to Placebo [2]		1.470		
LS SE Diff. to Placebo [2]		2.1726		
95% CI [2]		-2.829, 5.769		
One-sided p-value [2]		0.2499		
Hedge's G (95% CI)		0.12 [-0.247, 0.496]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	84.2	5.6	76.0	-2.9
SD	19.92	11.63	21.90	11.67
Median	93.3	0.0	80.0	0.0
Min, Max	0, 100	-20, 40	8, 100	-58, 27
LS Mean [2]		4.746		-3.047
LS SE [2]		1.8017		1.7795
95% CI [2]		1.185, 8.308		-6.565, 0.472
LS Mean Diff. to Placebo [2]		7.793		
LS SE Diff. to Placebo [2]		2.4732		
95% CI [2]		2.901, 12.685		
One-sided p-value [2]		0.0010		
Hedge's G (95% CI)		0.58 [0.202, 0.960]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	89.6	6.1	80.4	1.1
SD	13.95	8.18	19.24	13.09
Median	93.3	6.7	86.7	0.0
Min, Max	33, 100	-8, 33	33, 100	-33, 27
LS Mean [2]		7.397		1.237
LS SE [2]		1.6997		1.7557
95% CI [2]		4.029, 10.766		-2.243, 4.718
LS Mean Diff. to Placebo [2]		6.160		
LS SE Diff. to Placebo [2]		2.3810		
95% CI [2]		1.437, 10.883		
One-sided p-value [2]		0.0055		
Hedge's G (95% CI)		0.55 [0.110, 0.999]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	87.1	8.3	80.7	0.9
SD	17.05	13.16	19.66	8.91
Median	93.3	6.7	86.7	0.0
Min, Max	20, 100	-20, 40	20, 100	-27, 27
LS Mean [2]		7.293		1.321
LS SE [2]		1.6839		1.7070
95% CI [2]		3.960, 10.627		-2.058, 4.701
LS Mean Diff. to Placebo [2]		5.972		
LS SE Diff. to Placebo [2]		2.3335		
95% CI [2]		1.350, 10.594		
One-sided p-value [2]		0.0059		
Hedge's G (95% CI)		0.54 [0.108, 0.979]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	89.1	7.2	81.1	1.9
SD	15.06	11.72	18.75	12.16
Median	93.3	6.7	83.3	0.0
Min, Max	33, 100	-13, 33	27, 100	-33, 33
LS Mean [2]		7.524		2.110
LS SE [2]		1.5849		1.6261
95% CI [2]		4.385, 10.663		-1.110, 5.330
LS Mean Diff. to Placebo [2]		5.414		
LS SE Diff. to Placebo [2]		2.2040		
95% CI [2]		1.046, 9.782		
One-sided p-value [2]		0.0078		
Hedge's G (95% CI)		0.56 [0.090, 1.026]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	85.6	7.0	82.0	3.0
SD	20.62	13.41	16.17	8.35
Median	93.3	6.7	80.0	0.0
Min, Max	20, 100	-27, 33	40, 100	-7, 33
LS Mean [2]		6.197		2.257
LS SE [2]		1.7303		1.8179
95% CI [2]		2.770, 9.623		-1.343, 5.856
LS Mean Diff. to Placebo [2]		3.940		
LS SE Diff. to Placebo [2]		2.4472		
95% CI [2]		-0.909, 8.789		
One-sided p-value [2]		0.0551		
Hedge's G (95% CI)		0.35 [-0.093, 0.800]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	84.9	6.6	71.4	-2.0
SD	18.56	12.39	21.93	9.32
Median	93.3	6.7	66.7	0.0
Min, Max	27, 100	-20, 33	27, 100	-20, 13
LS Mean [2]		7.065		-2.145
LS SE [2]		1.6261		1.7913
95% CI [2]		3.844, 10.285		-5.692, 1.402
LS Mean Diff. to Placebo [2]		9.210		
LS SE Diff. to Placebo [2]		2.3583		
95% CI [2]		4.538, 13.882		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.90 [0.404, 1.390]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	87.0	8.0	76.0	0.4
SD	18.01	13.38	20.08	10.88
Median	93.3	6.7	80.0	0.0
Min, Max	13, 100	-20, 40	33, 100	-20, 20
LS Mean [2]		7.468		-0.663
LS SE [2]		1.7128		1.8651
95% CI [2]		4.077, 10.859		-4.354, 3.029
LS Mean Diff. to Placebo [2]		8.130		
LS SE Diff. to Placebo [2]		2.4727		
95% CI [2]		3.233, 13.028		
One-sided p-value [2]		0.0007		
Hedge's G (95% CI)		0.73 [0.267, 1.191]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	89.5	8.8	69.8	-3.8
SD	15.24	12.79	24.04	12.09
Median	93.3	6.7	73.3	0.0
Min, Max	27, 100	-7, 40	7, 100	-40, 27
LS Mean [2]		9.476		-5.377
LS SE [2]		1.8261		2.0277
95% CI [2]		5.855, 13.097		-9.397, -1.356
LS Mean Diff. to Placebo [2]		14.853		
LS SE Diff. to Placebo [2]		2.6780		
95% CI [2]		9.539, 20.166		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.35 [0.806, 1.885]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	87.8	8.4	72.8	-2.6
SD	19.52	15.51	19.86	9.44
Median	96.7	6.7	73.3	0.0
Min, Max	20, 100	-40, 40	20, 100	-27, 13
LS Mean [2]		8.833		-2.475
LS SE [2]		1.9791		2.1975
95% CI [2]		4.906, 12.760		-6.835, 1.884
LS Mean Diff. to Placebo [2]		11.309		
LS SE Diff. to Placebo [2]		2.9073		
95% CI [2]		5.537, 17.080		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.99 [0.452, 1.533]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	85.5	7.5	77.5	-2.5
SD	21.82	16.05	23.08	10.91
Median	93.3	6.7	80.0	0.0
Min, Max	27, 100	-33, 40	0, 100	-40, 20
LS Mean [2]		7.198		-3.447
LS SE [2]		2.2865		2.5776
95% CI [2]		2.661, 11.735		-8.560, 1.666
LS Mean Diff. to Placebo [2]		10.645		
LS SE Diff. to Placebo [2]		3.4029		
95% CI [2]		3.891, 17.400		
One-sided p-value [2]		0.0012		
Hedge's G (95% CI)		0.82 [0.276, 1.371]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	84.2	5.9	73.6	-5.2
SD	22.22	15.61	24.90	15.25
Median	93.3	6.7	80.0	0.0
Min, Max	13, 100	-33, 40	13, 100	-40, 27
LS Mean [2]		6.338		-3.148
LS SE [2]		2.2107		2.5607
95% CI [2]		1.954, 10.722		-8.224, 1.929
LS Mean Diff. to Placebo [2]		9.485		
LS SE Diff. to Placebo [2]		3.3376		
95% CI [2]		2.865, 16.106		
One-sided p-value [2]		0.0027		
Hedge's G (95% CI)		0.76 [0.205, 1.321]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	87.7	6.5	72.1	-1.6
SD	18.79	16.87	27.88	14.74
Median	93.3	6.7	73.3	0.0
Min, Max	33, 100	-47, 40	0, 100	-40, 33
LS Mean [2]		4.679		-3.924
LS SE [2]		2.3758		2.8039
95% CI [2]		-0.033, 9.392		-9.484, 1.637
LS Mean Diff. to Placebo [2]		8.603		
LS SE Diff. to Placebo [2]		3.6405		
95% CI [2]		1.381, 15.825		
One-sided p-value [2]		0.0100		
Hedge's G (95% CI)		0.64 [0.084, 1.205]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	84.5	8.0	73.0	-0.9
SD	20.54	17.08	25.86	14.15
Median	93.3	6.7	80.0	0.0
Min, Max	20, 100	-40, 47	0, 100	-40, 27
LS Mean [2]		7.209		-2.113
LS SE [2]		2.2418		2.6276
95% CI [2]		2.764, 11.653		-7.322, 3.095
LS Mean Diff. to Placebo [2]		9.322		
LS SE Diff. to Placebo [2]		3.4087		
95% CI [2]		2.562, 16.082		
One-sided p-value [2]		0.0037		
Hedge's G (95% CI)		0.75 [0.186, 1.316]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	88.2	7.8	78.1	-1.6
SD	19.07	14.54	18.22	12.65
Median	93.3	6.7	80.0	-3.3
Min, Max	13, 100	-20, 47	27, 100	-20, 33
LS Mean [2]		8.628		-0.430
LS SE [2]		2.0285		2.4739
95% CI [2]		4.603, 12.653		-5.338, 4.477
LS Mean Diff. to Placebo [2]		9.059		
LS SE Diff. to Placebo [2]		3.1574		
95% CI [2]		2.792, 15.325		
One-sided p-value [2]		0.0025		
Hedge's G (95% CI)		0.78 [0.212, 1.356]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	86.3	7.1	79.6	-1.4
SD	18.39	16.15	21.60	8.77
Median	96.7	3.3	86.7	0.0
Min, Max	33, 100	-27, 53	33, 100	-27, 13
LS Mean [2]		7.407		0.127
LS SE [2]		1.9188		2.3610
95% CI [2]		3.600, 11.215		-4.557, 4.812
LS Mean Diff. to Placebo [2]		7.280		
LS SE Diff. to Placebo [2]		2.9989		
95% CI [2]		1.328, 13.232		
One-sided p-value [2]		0.0085		
Hedge's G (95% CI)		0.68 [0.101, 1.266]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	86.8	8.4	75.0	-4.6
SD	19.60	14.83	23.18	8.33
Median	93.3	6.7	80.0	-6.7
Min, Max	20, 100	-20, 47	27, 100	-27, 7
LS Mean [2]		9.014		-3.135
LS SE [2]		1.8163		2.2713
95% CI [2]		5.412, 12.616		-7.639, 1.368
LS Mean Diff. to Placebo [2]		12.150		
LS SE Diff. to Placebo [2]		2.8614		
95% CI [2]		6.473, 17.826		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.19 [0.577, 1.795]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	90.7	8.2	83.0	-2.0
SD	14.99	15.89	13.38	11.00
Median	100.0	6.7	80.0	0.0
Min, Max	40, 100	-40, 40	60, 100	-27, 13
LS Mean [2]		7.892		-0.256
LS SE [2]		1.8164		2.3893
95% CI [2]		4.287, 11.496		-4.996, 4.484
LS Mean Diff. to Placebo [2]		8.148		
LS SE Diff. to Placebo [2]		2.9342		
95% CI [2]		2.323, 13.973		
One-sided p-value [2]		0.0033		
Hedge's G (95% CI)		0.80 [0.190, 1.401]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	86.4	8.9	83.3	-1.3
SD	20.45	15.40	13.98	7.78
Median	93.3	6.7	83.3	0.0
Min, Max	20, 100	-27, 47	60, 100	-20, 13
LS Mean [2]		7.480		1.480
LS SE [2]		2.0031		2.7002
95% CI [2]		3.499, 11.460		-3.886, 6.845
LS Mean Diff. to Placebo [2]		6.000		
LS SE Diff. to Placebo [2]		3.3285		
95% CI [2]		-0.617, 12.618		
One-sided p-value [2]		0.0375		
Hedge's G (95% CI)		0.54 [-0.076, 1.157]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	88.8	9.4	79.5	-1.9
SD	14.71	14.35	16.22	11.53
Median	93.3	6.7	80.0	0.0
Min, Max	53, 100	-27, 40	47, 100	-27, 13
LS Mean [2]		8.723		-0.203
LS SE [2]		1.5517		2.1788
95% CI [2]		5.646, 11.799		-4.522, 4.115
LS Mean Diff. to Placebo [2]		8.926		
LS SE Diff. to Placebo [2]		2.6247		
95% CI [2]		3.720, 14.132		
One-sided p-value [2]		0.0005		
Hedge's G (95% CI)		1.02 [0.359, 1.682]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	87.3	8.6	84.6	0.7
SD	16.54	15.03	13.34	9.13
Median	93.3	6.7	86.7	0.0
Min, Max	40, 100	-20, 47	60, 100	-13, 20
LS Mean [2]		8.074		2.175
LS SE [2]		1.5523		2.0771
95% CI [2]		4.994, 11.153		-1.945, 6.296
LS Mean Diff. to Placebo [2]		5.898		
LS SE Diff. to Placebo [2]		2.5463		
95% CI [2]		0.844, 10.953		
One-sided p-value [2]		0.0113		
Hedge's G (95% CI)		0.67 [0.084, 1.256]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	87.2	10.0	80.5	-3.6
SD	15.64	16.28	16.88	10.40
Median	93.3	6.7	80.0	0.0
Min, Max	50, 100	-30, 47	40, 100	-20, 13
LS Mean [2]		9.464		0.103
LS SE [2]		1.8170		2.5750
95% CI [2]		5.850, 13.077		-5.018, 5.224
LS Mean Diff. to Placebo [2]		9.361		
LS SE Diff. to Placebo [2]		3.1216		
95% CI [2]		3.149, 15.572		
One-sided p-value [2]		0.0018		
Hedge's G (95% CI)		0.95 [0.268, 1.638]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	89.8	7.9	82.4	-0.6
SD	18.57	12.04	16.94	12.09
Median	100.0	6.7	86.7	0.0
Min, Max	27, 100	-13, 33	40, 100	-20, 20
LS Mean [2]		7.766		0.678
LS SE [2]		1.9965		2.7843
95% CI [2]		3.762, 11.771		-4.906, 6.262
LS Mean Diff. to Placebo [2]		7.088		
LS SE Diff. to Placebo [2]		3.3808		
95% CI [2]		0.303, 13.874		
One-sided p-value [2]		0.0205		
Hedge's G (95% CI)		0.75 [0.000, 1.505]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	92.6	10.5	72.0	-5.3
SD	12.35	13.57	19.09	11.93
Median	100.0	6.7	73.3	-6.7
Min, Max	60, 100	-7, 40	40, 87	-20, 13
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	91.5	9.1	74.4	-5.6
SD	14.33	18.92	29.34	18.09
Median	100.0	0.0	76.7	0.0
Min, Max	53, 100	-20, 47	20, 100	-40, 13

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	90.0	11.1	83.3	3.3
SD	14.91	17.13	11.55	11.55
Median	96.7	6.7	80.0	0.0
Min, Max	60, 100	-7, 53	73, 100	-7, 20
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	88.9	8.3	86.7	0.0
SD	15.40	11.42	9.43	0.00
Median	96.7	6.7	86.7	0.0
Min, Max	53, 100	-7, 33	80, 93	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	87.9	12.7	80.0	-4.4
SD	13.27	16.18	6.67	3.85
Median	93.3	6.7	80.0	-6.7
Min, Max	53, 100	-7, 47	73, 87	-7, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	87.5	15.0	75.0	-5.0
SD	11.51	17.73	19.91	22.69
Median	93.3	16.7	73.3	-10.0
Min, Max	67, 100	-7, 47	53, 100	-27, 27

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	87.6	10.5	83.3	-6.7
SD	11.17	14.84	12.77	5.44
Median	93.3	13.3	80.0	-6.7
Min, Max	67, 100	-7, 27	73, 100	-13, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	84.4	13.3	93.3	-3.3
SD	9.11	16.33	9.43	4.71
Median	86.7	20.0	93.3	-3.3
Min, Max	67, 93	-7, 33	87, 100	-7, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	88.0	12.0		
SD	12.82	12.82		
Median	93.3	13.3		
Min, Max	67, 100	-7, 27		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	6.7		
SD	NA	NA		
Median	100.0	6.7		
Min, Max	100, 100	7, 7		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	6.7		
SD	NA	NA		
Median	100.0	6.7		
Min, Max	100, 100	7, 7		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	6.7		
SD	NA	NA		
Median	100.0	6.7		
Min, Max	100, 100	7, 7		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	53.3	-6.7		
SD	NA	NA		
Median	53.3	-6.7		
Min, Max	53, 53	-7, -7		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	82.9	2.9	86.7	-6.7
SD	28.77	6.51	NA	NA
Median	100.0	0.0	86.7	-6.7
Min, Max	27, 100	-7, 13	87, 87	-7, -7

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Role Functioning				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	64.8		65.7	
SD	32.67		30.15	
Median	66.7		66.7	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Role Functioning				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		9.722		-1.748
LS SE [2]		2.2129		2.3194
95% CI [2]		5.347, 14.097		-6.329, 2.832
LS Mean Diff. to Placebo [2]		11.470		
LS SE Diff. to Placebo [2]		3.0101		
95% CI [2]		5.521, 17.420		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		0.62 [0.271, 0.961]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	70.8	5.3	70.4	2.9
SD	30.63	17.76	27.28	23.51
Median	75.0	0.0	66.7	0.0
Min, Max	0, 100	-33, 50	0, 100	-33, 83
LS Mean [2]		2.945		1.459
LS SE [2]		3.0237		3.1384
95% CI [2]		-3.049, 8.939		-4.761, 7.679
LS Mean Diff. to Placebo [2]		1.486		
LS SE Diff. to Placebo [2]		4.2146		
95% CI [2]		-6.875, 9.846		
One-sided p-value [2]		0.3626		
Hedge's G (95% CI)		0.06 [-0.307, 0.436]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	76.7	11.6	65.3	-0.8
SD	25.18	23.25	26.85	21.76
Median	83.3	0.0	66.7	0.0
Min, Max	0, 100	-33, 67	0, 100	-67, 50
LS Mean [2]		8.162		-2.912
LS SE [2]		2.7756		2.7026
95% CI [2]		2.669, 13.655		-8.263, 2.439
LS Mean Diff. to Placebo [2]		11.074		
LS SE Diff. to Placebo [2]		3.7132		
95% CI [2]		3.719, 18.429		
One-sided p-value [2]		0.0017		
Hedge's G (95% CI)		0.54 [0.163, 0.918]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	83.0	14.5	69.8	-0.5
SD	21.51	23.99	28.56	25.66
Median	83.3	0.0	66.7	0.0
Min, Max	0, 100	-33, 83	17, 100	-67, 67
LS Mean [2]		10.929		1.195
LS SE [2]		3.4207		3.6446
95% CI [2]		4.132, 17.726		-6.045, 8.435
LS Mean Diff. to Placebo [2]		9.734		
LS SE Diff. to Placebo [2]		4.8740		
95% CI [2]		0.043, 19.425		
One-sided p-value [2]		0.0245		
Hedge's G (95% CI)		0.43 [-0.011, 0.871]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	81.4	14.0	70.7	1.2
SD	21.89	21.80	27.33	24.83
Median	83.3	0.0	66.7	0.0
Min, Max	17, 100	-17, 83	0, 100	-67, 83
LS Mean [2]		10.814		0.621
LS SE [2]		2.9939		3.0324
95% CI [2]		4.876, 16.753		-5.394, 6.636
LS Mean Diff. to Placebo [2]		10.193		
LS SE Diff. to Placebo [2]		4.1154		
95% CI [2]		2.023, 18.364		
One-sided p-value [2]		0.0075		
Hedge's G (95% CI)		0.52 [0.087, 0.957]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	78.9	7.5	72.2	1.0
SD	25.32	23.47	26.43	20.98
Median	83.3	0.0	75.0	0.0
Min, Max	17, 100	-33, 83	17, 100	-67, 33
LS Mean [2]		6.390		1.165
LS SE [2]		3.0917		3.1752
95% CI [2]		0.249, 12.531		-5.140, 7.469
LS Mean Diff. to Placebo [2]		5.226		
LS SE Diff. to Placebo [2]		4.2854		
95% CI [2]		-3.292, 13.744		
One-sided p-value [2]		0.1130		
Hedge's G (95% CI)		0.28 [-0.185, 0.737]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	77.9	11.6	68.0	0.9
SD	31.01	23.16	28.97	30.33
Median	100.0	0.0	66.7	0.0
Min, Max	0, 100	-33, 100	0, 100	-100, 67
LS Mean [2]		6.525		-0.675
LS SE [2]		3.4974		3.6738
95% CI [2]		-0.410, 13.459		-7.958, 6.608
LS Mean Diff. to Placebo [2]		7.199		
LS SE Diff. to Placebo [2]		4.9430		
95% CI [2]		-2.608, 17.007		
One-sided p-value [2]		0.0742		
Hedge's G (95% CI)		0.32 [-0.126, 0.765]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	79.1	13.2	59.4	-4.6
SD	26.00	24.28	30.22	16.60
Median	83.3	0.0	66.7	0.0
Min, Max	0, 100	-33, 83	0, 100	-33, 33
LS Mean [2]		11.446		-4.394
LS SE [2]		2.8151		3.1311
95% CI [2]		5.861, 17.032		-10.604, 1.815
LS Mean Diff. to Placebo [2]		15.841		
LS SE Diff. to Placebo [2]		4.0621		
95% CI [2]		7.777, 23.904		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.89 [0.395, 1.381]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	81.4	13.3	65.2	-2.9
SD	26.22	20.52	25.68	26.74
Median	100.0	0.0	66.7	0.0
Min, Max	0, 100	-17, 67	17, 100	-67, 50
LS Mean [2]		10.443		-1.627
LS SE [2]		2.8823		3.0913
95% CI [2]		4.731, 16.155		-7.751, 4.496
LS Mean Diff. to Placebo [2]		12.070		
LS SE Diff. to Placebo [2]		4.0705		
95% CI [2]		3.998, 20.142		
One-sided p-value [2]		0.0019		
Hedge's G (95% CI)		0.65 [0.188, 1.106]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	83.3	16.2	58.9	-6.5
SD	21.92	22.76	32.23	31.21
Median	100.0	8.3	58.3	0.0
Min, Max	33, 100	-17, 83	0, 100	-100, 50
LS Mean [2]		11.135		-5.545
LS SE [2]		3.1547		3.4476
95% CI [2]		4.878, 17.393		-12.381, 1.290
LS Mean Diff. to Placebo [2]		16.681		
LS SE Diff. to Placebo [2]		4.5350		
95% CI [2]		7.679, 25.682		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		0.88 [0.370, 1.391]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	81.4	13.2	64.1	-7.7
SD	27.14	26.20	23.89	25.05
Median	100.0	0.0	66.7	0.0
Min, Max	0, 100	-67, 67	33, 100	-67, 67
LS Mean [2]		10.319		-4.224
LS SE [2]		3.3509		3.6561
95% CI [2]		3.661, 16.976		-11.483, 3.035
LS Mean Diff. to Placebo [2]		14.542		
LS SE Diff. to Placebo [2]		4.8290		
95% CI [2]		4.941, 24.144		
One-sided p-value [2]		0.0017		
Hedge's G (95% CI)		0.76 [0.231, 1.287]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	75.3	11.1	75.7	6.9
SD	32.84	31.64	28.22	18.98
Median	100.0	0.0	83.3	0.0
Min, Max	0, 100	-50, 100	0, 100	-33, 67
LS Mean [2]		5.618		0.230
LS SE [2]		3.8586		4.2620
95% CI [2]		-2.052, 13.288		-8.236, 8.697
LS Mean Diff. to Placebo [2]		5.387		
LS SE Diff. to Placebo [2]		5.6398		
95% CI [2]		-5.828, 16.603		
One-sided p-value [2]		0.1711		
Hedge's G (95% CI)		0.25 [-0.279, 0.777]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	76.8	11.1	67.4	-1.5
SD	33.06	19.84	28.19	27.17
Median	100.0	0.0	66.7	0.0
Min, Max	0, 100	-33, 67	0, 100	-50, 83
LS Mean [2]		8.914		-1.217
LS SE [2]		3.0125		3.4362
95% CI [2]		2.932, 14.897		-8.034, 5.599
LS Mean Diff. to Placebo [2]		10.131		
LS SE Diff. to Placebo [2]		4.4306		
95% CI [2]		1.329, 18.934		
One-sided p-value [2]		0.0123		
Hedge's G (95% CI)		0.60 [0.050, 1.153]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	85.4	12.6	64.4	-5.6
SD	24.92	23.21	32.24	25.46
Median	100.0	0.0	66.7	0.0
Min, Max	0, 100	-33, 83	0, 100	-67, 50
LS Mean [2]		11.081		-3.406
LS SE [2]		2.8748		3.3107
95% CI [2]		5.381, 16.781		-9.967, 3.155
LS Mean Diff. to Placebo [2]		14.487		
LS SE Diff. to Placebo [2]		4.2350		
95% CI [2]		6.086, 22.889		
One-sided p-value [2]		0.0005		
Hedge's G (95% CI)		0.90 [0.332, 1.478]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	80.1	12.4	62.3	-4.5
SD	25.97	28.21	32.65	21.93
Median	100.0	0.0	66.7	0.0
Min, Max	17, 100	-67, 83	0, 100	-67, 33
LS Mean [2]		11.018		-3.644
LS SE [2]		3.2191		3.6297
95% CI [2]		4.627, 17.410		-10.847, 3.559
LS Mean Diff. to Placebo [2]		14.662		
LS SE Diff. to Placebo [2]		4.7217		
95% CI [2]		5.281, 24.044		
One-sided p-value [2]		0.0013		
Hedge's G (95% CI)		0.84 [0.266, 1.404]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	81.9	11.8	69.2	0.8
SD	28.24	22.67	30.72	27.29
Median	100.0	0.0	66.7	0.0
Min, Max	0, 100	-33, 67	0, 100	-67, 50
LS Mean [2]		10.658		0.345
LS SE [2]		2.9548		3.5137
95% CI [2]		4.795, 16.521		-6.623, 7.313
LS Mean Diff. to Placebo [2]		10.313		
LS SE Diff. to Placebo [2]		4.4578		
95% CI [2]		1.465, 19.162		
One-sided p-value [2]		0.0114		
Hedge's G (95% CI)		0.62 [0.053, 1.182]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	78.6	14.6	63.2	-14.0
SD	26.52	24.59	40.67	32.04
Median	83.3	8.3	83.3	0.0
Min, Max	0, 100	-33, 67	0, 100	-100, 33
LS Mean [2]		8.573		-10.888
LS SE [2]		3.4825		4.2042
95% CI [2]		1.662, 15.485		-19.228, -2.548
LS Mean Diff. to Placebo [2]		19.461		
LS SE Diff. to Placebo [2]		5.3648		
95% CI [2]		8.812, 30.111		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		1.01 [0.413, 1.614]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	81.3	14.6	65.8	-7.0
SD	25.60	27.88	34.40	24.42
Median	100.0	0.0	66.7	0.0
Min, Max	0, 100	-50, 83	0, 100	-67, 33
LS Mean [2]		10.801		-5.602
LS SE [2]		3.4132		4.1390
95% CI [2]		4.019, 17.584		-13.823, 2.618
LS Mean Diff. to Placebo [2]		16.404		
LS SE Diff. to Placebo [2]		5.2541		
95% CI [2]		5.958, 26.849		
One-sided p-value [2]		0.0012		
Hedge's G (95% CI)		0.86 [0.273, 1.449]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	86.9	16.2	75.0	-1.0
SD	23.11	25.17	23.74	21.63
Median	100.0	16.7	83.3	0.0
Min, Max	17, 100	-33, 67	33, 100	-50, 33
LS Mean [2]		14.359		-0.118
LS SE [2]		2.6106		3.2953
95% CI [2]		9.175, 19.543		-6.658, 6.422
LS Mean Diff. to Placebo [2]		14.477		
LS SE Diff. to Placebo [2]		4.0506		
95% CI [2]		6.430, 22.524		
One-sided p-value [2]		0.0003		
Hedge's G (95% CI)		1.00 [0.379, 1.612]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	81.7	13.3	71.9	0.0
SD	27.80	22.91	27.02	26.53
Median	100.0	0.0	83.3	0.0
Min, Max	0, 100	-17, 83	33, 100	-67, 50
LS Mean [2]		10.856		-0.303
LS SE [2]		2.8519		3.5278
95% CI [2]		5.197, 16.516		-7.307, 6.701
LS Mean Diff. to Placebo [2]		11.159		
LS SE Diff. to Placebo [2]		4.4014		
95% CI [2]		2.415, 19.904		
One-sided p-value [2]		0.0065		
Hedge's G (95% CI)		0.73 [0.101, 1.350]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	82.3	17.2	75.0	7.1
SD	23.16	27.59	29.05	29.75
Median	100.0	16.7	83.3	0.0
Min, Max	17, 100	-33, 100	17, 100	-33, 67
LS Mean [2]		11.684		2.037
LS SE [2]		3.3073		4.3569
95% CI [2]		5.106, 18.262		-6.622, 10.697
LS Mean Diff. to Placebo [2]		9.647		
LS SE Diff. to Placebo [2]		5.3602		
95% CI [2]		-1.018, 20.312		
One-sided p-value [2]		0.0378		
Hedge's G (95% CI)		0.53 [-0.111, 1.163]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	82.3	17.2	76.3	4.4
SD	23.93	23.37	27.95	26.55
Median	100.0	0.0	83.3	0.0
Min, Max	17, 100	-17, 67	17, 100	-67, 67
LS Mean [2]		12.951		1.784
LS SE [2]		2.6729		3.2300
95% CI [2]		7.647, 18.255		-4.622, 8.191
LS Mean Diff. to Placebo [2]		11.167		
LS SE Diff. to Placebo [2]		4.0687		
95% CI [2]		3.089, 19.244		
One-sided p-value [2]		0.0036		
Hedge's G (95% CI)		0.77 [0.175, 1.356]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	78.7	14.4	66.7	-6.4
SD	28.14	19.78	26.35	33.01
Median	100.0	0.0	66.7	-16.7
Min, Max	0, 100	-17, 67	17, 100	-83, 67
LS Mean [2]		11.221		-2.503
LS SE [2]		3.0647		4.0511
95% CI [2]		5.111, 17.330		-10.577, 5.571
LS Mean Diff. to Placebo [2]		13.724		
LS SE Diff. to Placebo [2]		4.9818		
95% CI [2]		3.785, 23.663		
One-sided p-value [2]		0.0038		
Hedge's G (95% CI)		0.84 [0.165, 1.522]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	81.0	10.3	63.6	-6.1
SD	28.52	26.60	30.57	32.72
Median	100.0	0.0	66.7	0.0
Min, Max	0, 100	-33, 67	17, 100	-83, 33
LS Mean [2]		6.761		-1.990
LS SE [2]		3.7839		4.8649
95% CI [2]		-0.809, 14.331		-11.725, 7.746
LS Mean Diff. to Placebo [2]		8.751		
LS SE Diff. to Placebo [2]		6.0717		
95% CI [2]		-3.408, 20.909		
One-sided p-value [2]		0.0775		
Hedge's G (95% CI)		0.50 [-0.237, 1.243]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	85.1	17.5	30.0	-26.7
SD	22.84	25.14	36.13	38.37
Median	100.0	16.7	16.7	0.0
Min, Max	17, 100	-17, 67	0, 83	-83, 0
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	83.3	18.2	52.8	-5.6
SD	25.82	27.34	40.02	31.03
Median	100.0	16.7	41.7	0.0
Min, Max	17, 100	-17, 83	0, 100	-50, 33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Role Functioning				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	81.9	22.2	58.3	8.3
SD	28.83	23.92	31.91	21.52
Median	100.0	16.7	50.0	8.3
Min, Max	17, 100	0, 83	33, 100	-17, 33
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	79.2	13.9	50.0	8.3
SD	29.41	19.89	70.71	11.79
Median	100.0	8.3	50.0	8.3
Min, Max	17, 100	0, 67	0, 100	0, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Role Functioning				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	72.7	18.2	61.1	11.1
SD	25.03	24.10	41.94	9.62
Median	66.7	16.7	66.7	16.7
Min, Max	17, 100	-17, 67	17, 100	0, 17
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	79.2	27.1	58.3	16.7
SD	17.25	26.63	41.94	33.33
Median	66.7	16.7	66.7	0.0
Min, Max	67, 100	0, 67	0, 100	0, 67

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Role Functioning				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	83.3	23.8	66.7	8.3
SD	16.67	35.82	27.22	21.52
Median	83.3	0.0	66.7	8.3
Min, Max	67, 100	0, 83	33, 100	-17, 33
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	77.8	30.6	83.3	0.0
SD	17.21	30.58	23.57	23.57
Median	66.7	25.0	83.3	0.0
Min, Max	67, 100	0, 67	67, 100	-17, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Role Functioning				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	83.3	30.0		
SD	16.67	41.50		
Median	83.3	0.0		
Min, Max	67, 100	0, 83		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	0.0		
SD	NA	NA		
Median	100.0	0.0		
Min, Max	100, 100	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Role Functioning				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	16.7		
SD	NA	NA		
Median	100.0	16.7		
Min, Max	100, 100	17, 17		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	16.7		
SD	NA	NA		
Median	100.0	16.7		
Min, Max	100, 100	17, 17		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Role Functioning				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	66.7	16.7		
SD	NA	NA		
Median	66.7	16.7		
Min, Max	67, 67	17, 17		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	69.0	9.5	33.3	-66.7
SD	35.26	25.20	NA	NA
Median	83.3	0.0	33.3	-66.7
Min, Max	17, 100	-17, 50	33, 33	-67, -67

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	46.7		47.9	
SD	30.77		32.71	
Median	33.3		33.3	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		-21.662		-2.331
LS SE [2]		2.5336		2.6341
95% CI [2]		-26.672, -16.651		-7.535, 2.874
LS Mean Diff. to Placebo [2]		-19.331		
LS SE Diff. to Placebo [2]		3.4016		
95% CI [2]		-26.057, -12.605		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.91 [-1.265, -0.556]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	33.6	-14.2	41.5	-4.2
SD	28.70	24.90	30.60	21.36
Median	33.3	-16.7	33.3	0.0
Min, Max	0, 100	-67, 50	0, 100	-50, 67
LS Mean [2]		-14.732		-4.725
LS SE [2]		3.2404		3.3376
95% CI [2]		-21.150, -8.315		-11.334, 1.885
LS Mean Diff. to Placebo [2]		-10.008		
LS SE Diff. to Placebo [2]		4.4543		
95% CI [2]		-18.835, -1.180		
One-sided p-value [2]		0.0133		
Hedge's G (95% CI)		-0.41 [-0.782, -0.031]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	26.1	-21.1	48.6	1.7
SD	25.00	29.63	32.35	25.28
Median	16.7	-16.7	50.0	0.0
Min, Max	0, 83	-100, 50	0, 100	-50, 83
LS Mean [2]		-19.908		0.081
LS SE [2]		3.3950		3.3369
95% CI [2]		-26.623, -13.194		-6.522, 6.684
LS Mean Diff. to Placebo [2]		-19.989		
LS SE Diff. to Placebo [2]		4.5633		
95% CI [2]		-29.022, -10.956		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.79 [-1.178, -0.408]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	22.1	-18.5	44.6	-2.8
SD	24.61	30.07	29.15	25.35
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 100	-83, 67	0, 100	-67, 50
LS Mean [2]		-20.747		-2.418
LS SE [2]		3.5335		3.6963
95% CI [2]		-27.749, -13.746		-9.741, 4.906
LS Mean Diff. to Placebo [2]		-18.330		
LS SE Diff. to Placebo [2]		4.9393		
95% CI [2]		-28.124, -8.536		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-0.79 [-1.243, -0.337]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	26.0	-19.4	44.3	-2.8
SD	25.01	25.70	29.72	24.97
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 100	-83, 17	0, 100	-50, 50
LS Mean [2]		-17.721		-0.374
LS SE [2]		3.2552		3.2952
95% CI [2]		-24.170, -11.272		-6.904, 6.155
LS Mean Diff. to Placebo [2]		-17.347		
LS SE Diff. to Placebo [2]		4.4314		
95% CI [2]		-26.134, -8.560		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.82 [-1.263, -0.372]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	25.0	-15.8	40.3	-2.4
SD	26.21	27.39	27.13	21.06
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 100	-83, 33	0, 100	-50, 33
LS Mean [2]		-17.368		-4.205
LS SE [2]		3.0962		3.1652
95% CI [2]		-23.506, -11.231		-10.476, 2.067
LS Mean Diff. to Placebo [2]		-13.164		
LS SE Diff. to Placebo [2]		4.2200		
95% CI [2]		-21.534, -4.793		
One-sided p-value [2]		0.0012		
Hedge's G (95% CI)		-0.70 [-1.169, -0.223]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	27.1	-20.5	39.2	-6.5
SD	29.78	30.39	30.23	24.00
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 100	-83, 50	0, 100	-83, 33
LS Mean [2]		-18.267		-4.324
LS SE [2]		3.5546		3.7029
95% CI [2]		-25.310, -11.224		-11.659, 3.012
LS Mean Diff. to Placebo [2]		-13.944		
LS SE Diff. to Placebo [2]		4.9470		
95% CI [2]		-23.753, -4.135		
One-sided p-value [2]		0.0029		
Hedge's G (95% CI)		-0.61 [-1.064, -0.158]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	27.9	-17.1	50.6	0.0
SD	28.57	28.52	30.16	18.37
Median	16.7	-16.7	50.0	0.0
Min, Max	0, 83	-100, 33	0, 100	-33, 50
LS Mean [2]		-19.282		0.964
LS SE [2]		3.2873		3.5932
95% CI [2]		-25.801, -12.763		-6.157, 8.085
LS Mean Diff. to Placebo [2]		-20.247		
LS SE Diff. to Placebo [2]		4.6829		
95% CI [2]		-29.536, -10.957		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.98 [-1.475, -0.481]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	23.1	-21.2	45.2	-2.0
SD	25.72	28.16	32.48	21.23
Median	16.7	-16.7	50.0	0.0
Min, Max	0, 100	-100, 17	0, 100	-50, 33
LS Mean [2]		-19.957		-1.648
LS SE [2]		3.2155		3.4210
95% CI [2]		-26.327, -13.587		-8.422, 5.125
LS Mean Diff. to Placebo [2]		-18.309		
LS SE Diff. to Placebo [2]		4.4944		
95% CI [2]		-27.217, -9.400		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.88 [-1.351, -0.414]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	21.9	-21.5	56.0	8.3
SD	24.23	28.19	36.07	25.86
Median	16.7	-16.7	50.0	0.0
Min, Max	0, 83	-83, 33	0, 100	-50, 67
LS Mean [2]		-22.363		6.998
LS SE [2]		3.3851		3.6512
95% CI [2]		-29.072, -15.654		-0.235, 14.231
LS Mean Diff. to Placebo [2]		-29.361		
LS SE Diff. to Placebo [2]		4.7955		
95% CI [2]		-38.872, -19.850		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.45 [-1.999, -0.904]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	21.6	-21.6	53.2	7.7
SD	28.29	28.29	34.00	25.92
Median	16.7	-16.7	50.0	0.0
Min, Max	0, 100	-83, 33	0, 100	-33, 67
LS Mean [2]		-20.729		2.319
LS SE [2]		3.5758		3.8566
95% CI [2]		-27.818, -13.639		-5.322, 9.960
LS Mean Diff. to Placebo [2]		-23.048		
LS SE Diff. to Placebo [2]		5.0816		
95% CI [2]		-33.129, -12.966		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.13 [-1.682, -0.583]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	22.7	-25.8	39.6	-3.5
SD	26.62	31.48	26.38	20.25
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-50, 33
LS Mean [2]		-21.291		-2.571
LS SE [2]		3.5204		3.8553
95% CI [2]		-28.282, -14.300		-10.220, 5.078
LS Mean Diff. to Placebo [2]		-18.720		
LS SE Diff. to Placebo [2]		5.0482		
95% CI [2]		-28.751, -8.689		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-0.95 [-1.505, -0.397]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	24.2	-20.2	44.2	1.5
SD	30.36	25.94	33.94	27.65
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 100	-83, 33	0, 100	-50, 67
LS Mean [2]		-21.530		1.899
LS SE [2]		4.0235		4.5142
95% CI [2]		-29.529, -13.532		-7.065, 10.864
LS Mean Diff. to Placebo [2]		-23.430		
LS SE Diff. to Placebo [2]		5.8923		
95% CI [2]		-35.149, -11.710		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.05 [-1.622, -0.474]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	16.2	-25.3	42.4	-4.0
SD	23.01	28.30	32.82	21.67
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 100	-83, 17	0, 100	-50, 33
LS Mean [2]		-24.164		-2.590
LS SE [2]		3.5591		4.0369
95% CI [2]		-31.236, -17.093		-10.606, 5.426
LS Mean Diff. to Placebo [2]		-21.574		
LS SE Diff. to Placebo [2]		5.2159		
95% CI [2]		-31.944, -11.204		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.09 [-1.679, -0.509]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	23.1	-23.7	45.7	-3.0
SD	26.41	25.01	35.25	20.98
Median	16.7	-33.3	33.3	0.0
Min, Max	0, 100	-67, 17	0, 100	-50, 33
LS Mean [2]		-22.552		-0.866
LS SE [2]		3.1886		3.5477
95% CI [2]		-28.878, -16.225		-7.901, 6.168
LS Mean Diff. to Placebo [2]		-21.685		
LS SE Diff. to Placebo [2]		4.5734		
95% CI [2]		-30.766, -12.605		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.25 [-1.849, -0.657]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	16.2	-22.5	40.0	-1.7
SD	23.74	27.18	36.83	25.31
Median	0.0	-16.7	33.3	0.0
Min, Max	0, 100	-83, 17	0, 100	-67, 33
LS Mean [2]		-24.737		0.522
LS SE [2]		3.3999		3.9491
95% CI [2]		-31.483, -17.990		-7.309, 8.353
LS Mean Diff. to Placebo [2]		-25.259		
LS SE Diff. to Placebo [2]		5.0232		
95% CI [2]		-35.232, -15.286		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.33 [-1.931, -0.719]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	19.8	-26.6	38.6	4.4
SD	26.25	32.20	35.60	18.29
Median	8.3	-25.0	33.3	0.0
Min, Max	0, 100	-100, 33	0, 100	-33, 33
LS Mean [2]		-22.950		0.761
LS SE [2]		3.2460		3.8390
95% CI [2]		-29.383, -16.517		-6.843, 8.366
LS Mean Diff. to Placebo [2]		-23.711		
LS SE Diff. to Placebo [2]		4.8590		
95% CI [2]		-33.344, -14.078		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.33 [-1.957, -0.710]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	19.7	-24.7	41.7	0.9
SD	24.46	29.79	33.11	26.34
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 83	-100, 17	0, 100	-50, 33
LS Mean [2]		-24.503		-3.881
LS SE [2]		3.2993		3.9147
95% CI [2]		-31.047, -17.959		-11.640, 3.877
LS Mean Diff. to Placebo [2]		-20.622		
LS SE Diff. to Placebo [2]		4.9391		
95% CI [2]		-30.423, -10.821		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.13 [-1.732, -0.523]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	15.7	-25.8	31.5	-3.9
SD	22.41	33.87	22.79	30.35
Median	0.0	-16.7	33.3	0.0
Min, Max	0, 83	-100, 33	0, 67	-50, 50
LS Mean [2]		-22.597		-1.959
LS SE [2]		3.3993		4.2221
95% CI [2]		-29.350, -15.843		-10.339, 6.422
LS Mean Diff. to Placebo [2]		-20.638		
LS SE Diff. to Placebo [2]		5.2286		
95% CI [2]		-31.030, -10.247		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.09 [-1.718, -0.472]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	21.7	-27.2	36.5	-3.1
SD	29.41	33.47	24.51	24.51
Median	16.7	-25.0	41.7	0.0
Min, Max	0, 100	-100, 33	0, 83	-50, 33
LS Mean [2]		-21.560		-4.337
LS SE [2]		3.4243		4.2456
95% CI [2]		-28.354, -14.767		-12.758, 4.084
LS Mean Diff. to Placebo [2]		-17.224		
LS SE Diff. to Placebo [2]		5.3051		
95% CI [2]		-27.756, -6.691		
One-sided p-value [2]		0.0008		
Hedge's G (95% CI)		-0.93 [-1.568, -0.296]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	15.1	-31.8	33.3	-9.5
SD	18.14	25.88	27.74	31.83
Median	16.7	-33.3	33.3	0.0
Min, Max	0, 67	-83, 17	0, 100	-83, 33
LS Mean [2]		-28.379		-11.499
LS SE [2]		2.6753		3.4789
95% CI [2]		-33.688, -23.069		-18.397, -4.602
LS Mean Diff. to Placebo [2]		-16.879		
LS SE Diff. to Placebo [2]		4.1856		
95% CI [2]		-25.189, -8.569		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.14 [-1.811, -0.471]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	19.4	-28.0	35.1	-7.0
SD	22.40	30.24	27.16	33.02
Median	16.7	-33.3	33.3	0.0
Min, Max	0, 67	-100, 33	0, 100	-83, 50
LS Mean [2]		-24.817		-7.065
LS SE [2]		3.0678		3.6925
95% CI [2]		-30.903, -18.730		-14.385, 0.255
LS Mean Diff. to Placebo [2]		-17.752		
LS SE Diff. to Placebo [2]		4.6265		
95% CI [2]		-26.933, -8.570		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		-1.06 [-1.670, -0.454]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	24.1	-23.0	44.9	6.4
SD	28.03	27.61	26.69	28.50
Median	16.7	-16.7	33.3	0.0
Min, Max	0, 100	-83, 33	0, 100	-33, 67
LS Mean [2]		-22.420		-3.352
LS SE [2]		3.4092		4.4942
95% CI [2]		-29.202, -15.639		-12.291, 5.587
LS Mean Diff. to Placebo [2]		-19.068		
LS SE Diff. to Placebo [2]		5.4977		
95% CI [2]		-30.014, -8.123		
One-sided p-value [2]		0.0004		
Hedge's G (95% CI)		-1.05 [-1.747, -0.363]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	11.9	-27.8	27.3	-9.1
SD	20.51	26.53	29.13	23.99
Median	0.0	-33.3	16.7	0.0
Min, Max	0, 67	-83, 17	0, 100	-50, 33
LS Mean [2]		-25.639		-11.333
LS SE [2]		3.0583		3.9618
95% CI [2]		-31.754, -19.525		-19.253, -3.413
LS Mean Diff. to Placebo [2]		-14.306		
LS SE Diff. to Placebo [2]		4.8126		
95% CI [2]		-23.938, -4.674		
One-sided p-value [2]		0.0021		
Hedge's G (95% CI)		-1.02 [-1.786, -0.245]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	11.4	-28.1	50.0	0.0
SD	20.07	27.25	42.49	20.41
Median	0.0	-33.3	50.0	0.0
Min, Max	0, 67	-83, 0	0, 100	-17, 33
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	18.2	-21.2	58.3	5.6
SD	20.35	25.92	25.28	27.22
Median	16.7	-16.7	58.3	8.3
Min, Max	0, 67	-67, 0	33, 100	-33, 33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	15.3	-26.4	54.2	0.0
SD	25.08	25.08	20.97	23.57
Median	0.0	-33.3	50.0	-8.3
Min, Max	0, 67	-83, 0	33, 83	-17, 33
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	20.8	-25.0	41.7	-16.7
SD	30.26	27.98	35.36	23.57
Median	0.0	-33.3	41.7	-16.7
Min, Max	0, 83	-83, 17	17, 67	-33, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	18.2	-31.8	38.9	-16.7
SD	26.30	31.14	25.46	16.67
Median	16.7	-33.3	33.3	-16.7
Min, Max	0, 83	-83, 17	17, 67	-33, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	14.6	-37.5	37.5	-37.5
SD	18.77	27.82	20.97	31.55
Median	8.3	-41.7	33.3	-25.0
Min, Max	0, 50	-67, 17	17, 67	-83, -17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	26.2	-23.8	37.5	-8.3
SD	21.21	25.20	8.33	31.91
Median	16.7	-33.3	33.3	0.0
Min, Max	0, 67	-67, 0	33, 50	-50, 17
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	19.4	-33.3	33.3	16.7
SD	19.48	33.33	0.00	0.00
Median	16.7	-33.3	33.3	16.7
Min, Max	0, 50	-83, 0	33, 33	17, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	23.3	-40.0		
SD	27.89	30.28		
Median	16.7	-33.3		
Min, Max	0, 67	-83, 0		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-50.0		
SD	NA	NA		
Median	0.0	-50.0		
Min, Max	0, 0	-50, -50		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Pain				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-33.3		
SD	NA	NA		
Median	0.0	-33.3		
Min, Max	0, 0	-33, -33		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-33.3		
SD	NA	NA		
Median	0.0	-33.3		
Min, Max	0, 0	-33, -33		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	33.3	-33.3		
SD	NA	NA		
Median	33.3	-33.3		
Min, Max	33, 33	-33, -33		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	50.0	-2.4	0.0	-16.7
SD	30.43	20.25	NA	NA
Median	50.0	0.0	0.0	-16.7
Min, Max	17, 100	-33, 33	0, 0	-17, -17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotional Functioning Scale				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	63.6		66.0	
SD	22.26		24.69	
Median	66.7		66.7	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotional Functioning Scale				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		9.307		2.022
LS SE [2]		1.9726		2.0987
95% CI [2]		5.406, 13.207		-2.123, 6.166
LS Mean Diff. to Placebo [2]		7.285		
LS SE Diff. to Placebo [2]		2.6998		
95% CI [2]		1.950, 12.621		
One-sided p-value [2]		0.0039		
Hedge's G (95% CI)		0.44 [0.094, 0.777]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotional Functioning Scale				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	67.5	4.9	71.2	4.0
SD	23.95	19.24	21.53	18.34
Median	75.0	4.2	75.0	0.0
Min, Max	0, 100	-50, 50	17, 100	-50, 50
LS Mean [2]		4.760		5.857
LS SE [2]		2.6498		2.7391
95% CI [2]		-0.485, 10.005		0.435, 11.278
LS Mean Diff. to Placebo [2]		-1.097		
LS SE Diff. to Placebo [2]		3.6788		
95% CI [2]		-8.384, 6.191		
One-sided p-value [2]		0.6169		
Hedge's G (95% CI)		-0.05 [-0.426, 0.317]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	71.3	6.7	69.1	3.8
SD	22.53	16.99	18.70	18.46
Median	75.0	8.3	66.7	0.0
Min, Max	0, 100	-50, 50	33, 100	-42, 42
LS Mean [2]		7.343		4.673
LS SE [2]		2.3600		2.2905
95% CI [2]		2.675, 12.011		0.140, 9.206
LS Mean Diff. to Placebo [2]		2.670		
LS SE Diff. to Placebo [2]		3.1329		
95% CI [2]		-3.533, 8.872		
One-sided p-value [2]		0.1979		
Hedge's G (95% CI)		0.15 [-0.218, 0.525]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	71.4	5.7	67.3	1.6
SD	23.69	21.44	18.98	20.10
Median	75.0	8.3	66.7	0.0
Min, Max	8, 100	-58, 42	33, 100	-33, 50
LS Mean [2]		4.468		4.589
LS SE [2]		2.9893		3.1722
95% CI [2]		-1.462, 10.397		-1.703, 10.880
LS Mean Diff. to Placebo [2]		-0.121		
LS SE Diff. to Placebo [2]		4.2379		
95% CI [2]		-8.533, 8.291		
One-sided p-value [2]		0.5114		
Hedge's G (95% CI)		-0.01 [-0.442, 0.430]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	72.1	7.8	68.5	1.8
SD	18.98	22.38	18.12	20.11
Median	66.7	8.3	66.7	0.0
Min, Max	25, 100	-42, 58	33, 100	-42, 50
LS Mean [2]		6.071		5.007
LS SE [2]		2.6101		2.6440
95% CI [2]		0.900, 11.242		-0.232, 10.246
LS Mean Diff. to Placebo [2]		1.064		
LS SE Diff. to Placebo [2]		3.5753		
95% CI [2]		-6.025, 8.154		
One-sided p-value [2]		0.3833		
Hedge's G (95% CI)		0.06 [-0.365, 0.490]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	73.0	5.7	69.9	2.1
SD	22.96	20.70	19.14	21.52
Median	75.0	0.0	66.7	0.0
Min, Max	25, 100	-42, 50	33, 100	-42, 50
LS Mean [2]		6.161		4.949
LS SE [2]		2.7318		2.7921
95% CI [2]		0.748, 11.574		-0.581, 10.480
LS Mean Diff. to Placebo [2]		1.212		
LS SE Diff. to Placebo [2]		3.7682		
95% CI [2]		-6.260, 8.683		
One-sided p-value [2]		0.3742		
Hedge's G (95% CI)		0.07 [-0.387, 0.532]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	72.3	7.9	66.2	5.3
SD	23.97	21.20	16.66	21.10
Median	75.0	8.3	66.7	4.2
Min, Max	0, 100	-50, 58	25, 100	-33, 67
LS Mean [2]		7.357		3.013
LS SE [2]		2.5495		2.6868
95% CI [2]		2.309, 12.404		-2.306, 8.333
LS Mean Diff. to Placebo [2]		4.343		
LS SE Diff. to Placebo [2]		3.5551		
95% CI [2]		-2.701, 11.388		
One-sided p-value [2]		0.1122		
Hedge's G (95% CI)		0.26 [-0.181, 0.709]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	71.2	7.4	66.0	1.6
SD	22.46	20.76	22.12	19.47
Median	75.0	8.3	66.7	0.0
Min, Max	0, 100	-33, 67	25, 100	-33, 67
LS Mean [2]		7.432		2.261
LS SE [2]		2.5773		2.8636
95% CI [2]		2.324, 12.540		-3.413, 7.934
LS Mean Diff. to Placebo [2]		5.171		
LS SE Diff. to Placebo [2]		3.7145		
95% CI [2]		-2.194, 12.537		
One-sided p-value [2]		0.0834		
Hedge's G (95% CI)		0.32 [-0.157, 0.791]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	76.9	11.9	63.1	-5.1
SD	18.32	20.13	21.42	20.31
Median	79.2	8.3	66.7	-4.2
Min, Max	25, 100	-33, 58	8, 100	-50, 50
LS Mean [2]		8.821		-1.058
LS SE [2]		2.5605		2.7630
95% CI [2]		3.749, 13.894		-6.530, 4.413
LS Mean Diff. to Placebo [2]		9.880		
LS SE Diff. to Placebo [2]		3.6273		
95% CI [2]		2.689, 17.070		
One-sided p-value [2]		0.0038		
Hedge's G (95% CI)		0.59 [0.138, 1.052]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	74.1	8.1	56.0	-8.0
SD	23.15	23.85	27.58	22.74
Median	75.0	8.3	62.5	-4.2
Min, Max	0, 100	-50, 75	0, 100	-67, 33
LS Mean [2]		5.536		-5.035
LS SE [2]		3.2509		3.5820
95% CI [2]		-0.912, 11.984		-12.137, 2.067
LS Mean Diff. to Placebo [2]		10.572		
LS SE Diff. to Placebo [2]		4.7287		
95% CI [2]		1.187, 19.956		
One-sided p-value [2]		0.0138		
Hedge's G (95% CI)		0.54 [0.043, 1.036]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	74.0	7.4	65.4	-3.8
SD	21.10	22.17	21.56	18.89
Median	75.0	0.0	66.7	0.0
Min, Max	17, 100	-50, 58	8, 100	-42, 33
LS Mean [2]		8.027		2.142
LS SE [2]		2.9287		3.2310
95% CI [2]		2.211, 13.842		-4.270, 8.554
LS Mean Diff. to Placebo [2]		5.884		
LS SE Diff. to Placebo [2]		4.2307		
95% CI [2]		-2.523, 14.291		
One-sided p-value [2]		0.0839		
Hedge's G (95% CI)		0.35 [-0.165, 0.864]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotional Functioning Scale				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	68.2	4.8	65.6	-3.1
SD	24.78	22.44	23.35	19.78
Median	66.7	0.0	66.7	0.0
Min, Max	17, 100	-50, 42	0, 100	-58, 33
LS Mean [2]		4.439		-0.550
LS SE [2]		3.0513		3.4068
95% CI [2]		-1.616, 10.493		-7.306, 6.206
LS Mean Diff. to Placebo [2]		4.989		
LS SE Diff. to Placebo [2]		4.4686		
95% CI [2]		-3.883, 13.861		
One-sided p-value [2]		0.1335		
Hedge's G (95% CI)		0.29 [-0.238, 0.819]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	70.7	7.8	65.2	-4.5
SD	27.01	23.75	20.20	24.22
Median	83.3	8.3	66.7	-8.3
Min, Max	0, 100	-33, 67	17, 100	-50, 67
LS Mean [2]		7.952		0.295
LS SE [2]		3.1705		3.6596
95% CI [2]		1.656, 14.249		-6.967, 7.557
LS Mean Diff. to Placebo [2]		7.657		
LS SE Diff. to Placebo [2]		4.7470		
95% CI [2]		-1.774, 17.089		
One-sided p-value [2]		0.0551		
Hedge's G (95% CI)		0.43 [-0.115, 0.975]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	78.1	9.2	64.4	-7.1
SD	21.92	20.73	27.60	22.71
Median	83.3	8.3	70.8	0.0
Min, Max	25, 100	-42, 42	0, 100	-58, 33
LS Mean [2]		11.320		-1.320
LS SE [2]		3.5179		4.1273
95% CI [2]		4.318, 18.321		-9.532, 6.891
LS Mean Diff. to Placebo [2]		12.640		
LS SE Diff. to Placebo [2]		5.2862		
95% CI [2]		2.113, 23.167		
One-sided p-value [2]		0.0096		
Hedge's G (95% CI)		0.64 [0.081, 1.201]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	78.5	12.1	60.5	-6.4
SD	20.04	20.28	26.73	25.19
Median	83.3	16.7	66.7	0.0
Min, Max	25, 100	-33, 58	0, 100	-58, 50
LS Mean [2]		13.299		-2.697
LS SE [2]		3.1998		3.6501
95% CI [2]		6.939, 19.658		-9.949, 4.555
LS Mean Diff. to Placebo [2]		15.996		
LS SE Diff. to Placebo [2]		4.7480		
95% CI [2]		6.552, 25.439		
One-sided p-value [2]		0.0006		
Hedge's G (95% CI)		0.91 [0.339, 1.486]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotional Functioning Scale				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	73.8	7.6	58.3	-5.8
SD	25.88	26.38	24.78	22.47
Median	83.3	8.3	62.5	-4.2
Min, Max	17, 100	-42, 50	0, 100	-58, 42
LS Mean [2]		6.294		-1.187
LS SE [2]		3.6357		4.3952
95% CI [2]		-0.936, 13.525		-9.924, 7.549
LS Mean Diff. to Placebo [2]		7.482		
LS SE Diff. to Placebo [2]		5.6127		
95% CI [2]		-3.683, 18.647		
One-sided p-value [2]		0.0931		
Hedge's G (95% CI)		0.36 [-0.194, 0.919]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	76.3	12.2	65.8	-6.6
SD	20.42	20.19	21.14	13.49
Median	75.0	12.5	66.7	-8.3
Min, Max	33, 100	-33, 50	33, 100	-33, 25
LS Mean [2]		11.604		-2.016
LS SE [2]		2.5857		3.1468
95% CI [2]		6.463, 16.744		-8.272, 4.241
LS Mean Diff. to Placebo [2]		13.619		
LS SE Diff. to Placebo [2]		3.9825		
95% CI [2]		5.697, 21.541		
One-sided p-value [2]		0.0005		
Hedge's G (95% CI)		0.95 [0.355, 1.549]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	77.5	10.4	66.3	-5.3
SD	21.19	20.09	25.29	21.91
Median	83.3	8.3	66.7	0.0
Min, Max	25, 100	-50, 50	0, 100	-58, 33
LS Mean [2]		10.998		2.707
LS SE [2]		2.9386		3.6360
95% CI [2]		5.162, 16.834		-4.511, 9.926
LS Mean Diff. to Placebo [2]		8.291		
LS SE Diff. to Placebo [2]		4.5528		
95% CI [2]		-0.756, 17.338		
One-sided p-value [2]		0.0360		
Hedge's G (95% CI)		0.50 [-0.071, 1.075]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	78.0	12.1	62.5	-9.3
SD	21.53	21.36	24.13	23.73
Median	83.3	8.3	66.7	0.0
Min, Max	25, 100	-33, 67	0, 100	-58, 33
LS Mean [2]		11.378		-1.497
LS SE [2]		3.1016		4.0040
95% CI [2]		5.211, 17.545		-9.455, 6.461
LS Mean Diff. to Placebo [2]		12.875		
LS SE Diff. to Placebo [2]		4.9670		
95% CI [2]		2.995, 22.755		
One-sided p-value [2]		0.0056		
Hedge's G (95% CI)		0.74 [0.137, 1.343]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	75.3	10.8	66.7	-0.5
SD	24.22	26.73	24.15	27.13
Median	75.0	8.3	70.8	0.0
Min, Max	0, 100	-50, 83	17, 100	-42, 75
LS Mean [2]		10.353		2.854
LS SE [2]		3.2784		4.2243
95% CI [2]		3.840, 16.865		-5.538, 11.246
LS Mean Diff. to Placebo [2]		7.499		
LS SE Diff. to Placebo [2]		5.2612		
95% CI [2]		-2.960, 17.957		
One-sided p-value [2]		0.0788		
Hedge's G (95% CI)		0.42 [-0.194, 1.031]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	79.2	13.5	71.4	5.4
SD	22.10	21.46	20.86	27.27
Median	83.3	16.7	70.8	0.0
Min, Max	33, 100	-42, 50	33, 100	-33, 75
LS Mean [2]		13.815		8.448
LS SE [2]		2.9251		4.0048
95% CI [2]		8.002, 19.629		0.492, 16.405
LS Mean Diff. to Placebo [2]		5.367		
LS SE Diff. to Placebo [2]		4.8616		
95% CI [2]		-4.301, 15.034		
One-sided p-value [2]		0.1364		
Hedge's G (95% CI)		0.33 [-0.304, 0.959]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotional Functioning Scale				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	78.5	15.6	70.2	3.5
SD	24.23	22.95	23.95	27.54
Median	83.3	16.7	66.7	0.0
Min, Max	8, 100	-50, 58	17, 100	-50, 83
LS Mean [2]		14.280		1.961
LS SE [2]		3.3878		4.2228
95% CI [2]		7.544, 21.017		-6.434, 10.357
LS Mean Diff. to Placebo [2]		12.319		
LS SE Diff. to Placebo [2]		5.3365		
95% CI [2]		1.702, 22.936		
One-sided p-value [2]		0.0118		
Hedge's G (95% CI)		0.66 [0.074, 1.245]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	79.0	14.7	69.9	1.9
SD	24.86	20.13	21.66	20.17
Median	91.7	8.3	75.0	0.0
Min, Max	0, 100	-42, 58	25, 100	-42, 33
LS Mean [2]		16.636		4.624
LS SE [2]		2.8716		3.9579
95% CI [2]		10.918, 22.354		-3.260, 12.508
LS Mean Diff. to Placebo [2]		12.012		
LS SE Diff. to Placebo [2]		4.8020		
95% CI [2]		2.440, 21.584		
One-sided p-value [2]		0.0073		
Hedge's G (95% CI)		0.78 [0.105, 1.455]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	84.5	20.6	75.0	5.3
SD	20.80	17.40	17.08	20.16
Median	91.7	16.7	75.0	0.0
Min, Max	33, 100	-8, 58	42, 100	-25, 42
LS Mean [2]		15.714		8.478
LS SE [2]		3.2106		4.3329
95% CI [2]		9.260, 22.168		-0.231, 17.187
LS Mean Diff. to Placebo [2]		7.236		
LS SE Diff. to Placebo [2]		5.3440		
95% CI [2]		-3.515, 17.987		
One-sided p-value [2]		0.0911		
Hedge's G (95% CI)		0.48 [-0.256, 1.222]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotional Functioning Scale				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	85.1	17.5	51.7	-11.7
SD	17.03	16.87	29.70	27.39
Median	91.7	16.7	58.3	-8.3
Min, Max	42, 100	-8, 50	0, 75	-58, 8
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	77.8	15.7	59.7	-15.3
SD	15.86	11.27	35.52	30.47
Median	75.0	16.7	70.8	0.0
Min, Max	50, 100	0, 33	8, 100	-58, 8

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotional Functioning Scale				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	86.6	24.8	58.3	-8.3
SD	18.57	20.43	28.87	22.57
Median	95.8	25.0	66.7	0.0
Min, Max	42, 100	-8, 58	17, 83	-42, 8
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	76.4	13.2	50.0	-8.3
SD	19.73	17.57	35.36	35.36
Median	79.2	12.5	50.0	-8.3
Min, Max	42, 100	-17, 42	25, 75	-33, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotional Functioning Scale				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	84.1	21.2	52.8	-8.3
SD	14.65	22.78	17.35	14.43
Median	91.7	25.0	58.3	0.0
Min, Max	50, 100	-17, 50	33, 67	-25, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	88.5	28.1	50.0	0.0
SD	10.85	17.78	43.03	65.62
Median	87.5	29.2	50.0	-16.7
Min, Max	75, 100	0, 58	0, 100	-58, 92

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	79.8	15.5	56.3	-8.3
SD	11.64	12.20	19.69	15.21
Median	75.0	25.0	50.0	-8.3
Min, Max	67, 100	0, 25	42, 83	-25, 8
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	91.7	29.2	79.2	12.5
SD	9.13	17.28	17.68	5.89
Median	91.7	29.2	79.2	12.5
Min, Max	75, 100	8, 50	67, 92	8, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	75.0	13.3		
SD	11.79	11.18		
Median	75.0	8.3		
Min, Max	58, 92	0, 25		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	91.7	25.0		
SD	NA	NA		
Median	91.7	25.0		
Min, Max	92, 92	25, 25		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	33.3		
SD	NA	NA		
Median	100.0	33.3		
Min, Max	100, 100	33, 33		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	33.3		
SD	NA	NA		
Median	100.0	33.3		
Min, Max	100, 100	33, 33		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Emotional Functioning Scale				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	83.3	41.7		
SD	NA	NA		
Median	83.3	41.7		
Min, Max	83, 83	42, 42		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	66.7	6.0	66.7	16.7
SD	31.91	9.27	NA	NA
Median	66.7	0.0	66.7	16.7
Min, Max	8, 100	0, 25	67, 67	17, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	81.2		84.3	
SD	26.45		19.84	
Median	83.3		83.3	
Min, Max	0, 100		17, 100	

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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		-5.293		-1.381
LS SE [2]		1.8077		1.9138
95% CI [2]		-8.868, -1.718		-5.161, 2.398
LS Mean Diff. to Placebo [2]		-3.912		
LS SE Diff. to Placebo [2]		2.4821		
95% CI [2]		-8.818, 0.994		
One-sided p-value [2]		0.9414		
Hedge's G (95% CI)		-0.26 [-0.595, 0.083]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	79.2	-2.5	85.5	2.2
SD	25.79	19.85	19.35	13.62
Median	83.3	0.0	100.0	0.0
Min, Max	0, 100	-83, 33	33, 100	-50, 33
LS Mean [2]		-3.633		1.570
LS SE [2]		2.4649		2.5583
95% CI [2]		-8.516, 1.250		-3.497, 6.637
LS Mean Diff. to Placebo [2]		-5.203		
LS SE Diff. to Placebo [2]		3.4272		
95% CI [2]		-11.997, 1.590		
One-sided p-value [2]		0.9341		
Hedge's G (95% CI)		-0.28 [-0.650, 0.096]		

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	79.9	-1.6	87.3	1.7
SD	25.18	16.75	17.87	14.42
Median	83.3	0.0	100.0	0.0
Min, Max	0, 100	-50, 67	33, 100	-50, 33
LS Mean [2]		-2.364		1.284
LS SE [2]		2.1480		2.0650
95% CI [2]		-6.615, 1.887		-2.805, 5.373
LS Mean Diff. to Placebo [2]		-3.648		
LS SE Diff. to Placebo [2]		2.8432		
95% CI [2]		-9.280, 1.984		
One-sided p-value [2]		0.8990		
Hedge's G (95% CI)		-0.23 [-0.604, 0.141]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	79.7	-3.3	84.7	0.9
SD	22.47	28.03	18.99	17.79
Median	83.3	0.0	83.3	0.0
Min, Max	17, 100	-50, 100	33, 100	-50, 33
LS Mean [2]		-5.636		-1.125
LS SE [2]		3.2242		3.4506
95% CI [2]		-12.040, 0.769		-7.977, 5.728
LS Mean Diff. to Placebo [2]		-4.511		
LS SE Diff. to Placebo [2]		4.6240		
95% CI [2]		-13.702, 4.680		
One-sided p-value [2]		0.8340		
Hedge's G (95% CI)		-0.21 [-0.648, 0.226]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	74.8	-5.8	83.3	-3.3
SD	26.82	21.48	24.44	22.43
Median	83.3	0.0	100.0	0.0
Min, Max	0, 100	-67, 50	0, 100	-83, 33
LS Mean [2]		-6.626		-1.973
LS SE [2]		3.1176		3.1393
95% CI [2]		-12.805, -0.447		-8.195, 4.249
LS Mean Diff. to Placebo [2]		-4.654		
LS SE Diff. to Placebo [2]		4.3338		
95% CI [2]		-13.248, 3.941		
One-sided p-value [2]		0.8573		
Hedge's G (95% CI)		-0.23 [-0.659, 0.200]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	77.6	-3.1	87.5	-1.0
SD	20.97	24.15	14.57	14.54
Median	75.0	0.0	91.7	0.0
Min, Max	17, 100	-50, 67	50, 100	-33, 33
LS Mean [2]		-6.896		1.476
LS SE [2]		2.5568		2.6164
95% CI [2]		-11.975, -1.816		-3.720, 6.672
LS Mean Diff. to Placebo [2]		-8.372		
LS SE Diff. to Placebo [2]		3.5631		
95% CI [2]		-15.455, -1.289		
One-sided p-value [2]		0.9895		
Hedge's G (95% CI)		-0.54 [-1.003, -0.068]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Cognitive Functioning Scale				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	75.6	-3.9	91.0	1.9
SD	27.54	23.80	13.38	16.80
Median	83.3	0.0	100.0	0.0
Min, Max	0, 100	-83, 33	50, 100	-33, 33
LS Mean [2]		-5.179		3.532
LS SE [2]		2.8332		2.9538
95% CI [2]		-10.800, 0.441		-2.327, 9.391
LS Mean Diff. to Placebo [2]		-8.712		
LS SE Diff. to Placebo [2]		4.0126		
95% CI [2]		-16.677, -0.746		
One-sided p-value [2]		0.9838		
Hedge's G (95% CI)		-0.48 [-0.928, -0.030]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	76.7	-3.1	90.6	0.0
SD	26.01	19.67	13.62	14.77
Median	83.3	0.0	100.0	0.0
Min, Max	0, 100	-33, 50	50, 100	-33, 33
LS Mean [2]		-4.044		3.135
LS SE [2]		2.3923		2.6722
95% CI [2]		-8.793, 0.705		-2.166, 8.437
LS Mean Diff. to Placebo [2]		-7.179		
LS SE Diff. to Placebo [2]		3.5055		
95% CI [2]		-14.140, -0.218		
One-sided p-value [2]		0.9783		
Hedge's G (95% CI)		-0.47 [-0.950, 0.004]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	79.2	-3.8	84.3	-3.4
SD	22.77	24.08	21.37	23.49
Median	83.3	0.0	100.0	0.0
Min, Max	17, 100	-67, 67	17, 100	-67, 67
LS Mean [2]		-5.726		1.409
LS SE [2]		2.7201		2.9296
95% CI [2]		-11.113, -0.339		-4.391, 7.208
LS Mean Diff. to Placebo [2]		-7.135		
LS SE Diff. to Placebo [2]		3.8958		
95% CI [2]		-14.854, 0.584		
One-sided p-value [2]		0.9652		
Hedge's G (95% CI)		-0.40 [-0.857, 0.047]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	77.2	-9.6	80.4	-7.1
SD	25.24	24.08	22.70	23.32
Median	83.3	0.0	83.3	0.0
Min, Max	17, 100	-67, 33	0, 100	-83, 33
LS Mean [2]		-8.930		-1.871
LS SE [2]		3.1267		3.4557
95% CI [2]		-15.132, -2.728		-8.723, 4.981
LS Mean Diff. to Placebo [2]		-7.059		
LS SE Diff. to Placebo [2]		4.5655		
95% CI [2]		-16.119, 2.001		
One-sided p-value [2]		0.9374		
Hedge's G (95% CI)		-0.37 [-0.867, 0.118]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	80.4	-4.9	85.9	-4.5
SD	24.44	19.48	18.07	14.57
Median	91.7	0.0	100.0	0.0
Min, Max	0, 100	-67, 33	33, 100	-33, 33
LS Mean [2]		-3.762		-2.631
LS SE [2]		2.8429		3.1504
95% CI [2]		-9.416, 1.892		-8.893, 3.631
LS Mean Diff. to Placebo [2]		-1.131		
LS SE Diff. to Placebo [2]		4.1457		
95% CI [2]		-9.383, 7.121		
One-sided p-value [2]		0.6072		
Hedge's G (95% CI)		-0.07 [-0.580, 0.442]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	75.8	-7.1	80.6	-7.6
SD	23.97	27.65	18.17	17.71
Median	83.3	0.0	83.3	-8.3
Min, Max	17, 100	-67, 83	50, 100	-50, 17
LS Mean [2]		-7.432		-2.977
LS SE [2]		3.2257		3.6076
95% CI [2]		-13.850, -1.014		-10.151, 4.197
LS Mean Diff. to Placebo [2]		-4.455		
LS SE Diff. to Placebo [2]		4.7697		
95% CI [2]		-13.950, 5.041		
One-sided p-value [2]		0.8234		
Hedge's G (95% CI)		-0.25 [-0.773, 0.283]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	72.7	-10.1	83.3	-8.3
SD	26.62	23.18	16.67	17.63
Median	66.7	0.0	83.3	0.0
Min, Max	0, 100	-67, 50	50, 100	-50, 17
LS Mean [2]		-7.173		-3.354
LS SE [2]		2.8869		3.3580
95% CI [2]		-12.909, -1.437		-10.020, 3.313
LS Mean Diff. to Placebo [2]		-3.819		
LS SE Diff. to Placebo [2]		4.3583		
95% CI [2]		-12.482, 4.844		
One-sided p-value [2]		0.8084		
Hedge's G (95% CI)		-0.23 [-0.776, 0.306]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Cognitive Functioning Scale				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	79.3	-6.1	81.1	-9.5
SD	25.36	19.01	18.75	13.51
Median	83.3	0.0	83.3	-16.7
Min, Max	0, 100	-67, 33	33, 100	-33, 17
LS Mean [2]		-5.673		-7.629
LS SE [2]		2.6327		3.1140
95% CI [2]		-10.907, -0.440		-13.818, -1.441
LS Mean Diff. to Placebo [2]		1.956		
LS SE Diff. to Placebo [2]		3.9840		
95% CI [2]		-5.969, 9.881		
One-sided p-value [2]		0.3124		
Hedge's G (95% CI)		0.13 [-0.416, 0.680]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	78.5	-3.8	86.2	-7.6
SD	23.65	19.58	18.57	20.40
Median	83.3	0.0	100.0	0.0
Min, Max	17, 100	-50, 33	50, 100	-50, 33
LS Mean [2]		-3.299		-2.884
LS SE [2]		2.8222		3.2671
95% CI [2]		-8.910, 2.311		-9.377, 3.609
LS Mean Diff. to Placebo [2]		-0.416		
LS SE Diff. to Placebo [2]		4.2597		
95% CI [2]		-8.891, 8.059		
One-sided p-value [2]		0.5387		
Hedge's G (95% CI)		-0.03 [-0.573, 0.520]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	81.9	-5.4	83.3	-6.7
SD	22.98	20.40	15.29	11.34
Median	83.3	0.0	83.3	0.0
Min, Max	0, 100	-67, 33	67, 100	-33, 0
LS Mean [2]		-4.995		0.241
LS SE [2]		2.8258		3.4438
95% CI [2]		-10.626, 0.636		-6.618, 7.100
LS Mean Diff. to Placebo [2]		-5.236		
LS SE Diff. to Placebo [2]		4.3563		
95% CI [2]		-13.922, 3.450		
One-sided p-value [2]		0.8833		
Hedge's G (95% CI)		-0.33 [-0.881, 0.230]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	82.3	-3.1	86.8	-5.3
SD	18.42	18.18	15.29	7.96
Median	83.3	0.0	100.0	0.0
Min, Max	33, 100	-33, 33	67, 100	-17, 0
LS Mean [2]		-3.119		-1.764
LS SE [2]		2.1131		2.5718
95% CI [2]		-7.323, 1.084		-6.882, 3.353
LS Mean Diff. to Placebo [2]		-1.355		
LS SE Diff. to Placebo [2]		3.2290		
95% CI [2]		-7.783, 5.074		
One-sided p-value [2]		0.6620		
Hedge's G (95% CI)		-0.12 [-0.684, 0.452]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	79.3	-6.6	82.5	-9.6
SD	20.00	23.18	20.57	16.02
Median	83.3	0.0	83.3	0.0
Min, Max	33, 100	-67, 50	17, 100	-50, 17
LS Mean [2]		-6.003		-2.484
LS SE [2]		2.7316		3.4032
95% CI [2]		-11.431, -0.575		-9.245, 4.276
LS Mean Diff. to Placebo [2]		-3.518		
LS SE Diff. to Placebo [2]		4.2738		
95% CI [2]		-12.017, 4.980		
One-sided p-value [2]		0.7937		
Hedge's G (95% CI)		-0.23 [-0.795, 0.338]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	83.3	-5.6	78.7	-11.8
SD	20.83	26.24	19.64	16.42
Median	100.0	0.0	83.3	-16.7
Min, Max	33, 100	-67, 67	33, 100	-50, 17
LS Mean [2]		-3.800		-5.818
LS SE [2]		2.8289		3.6197
95% CI [2]		-9.418, 1.819		-13.004, 1.369
LS Mean Diff. to Placebo [2]		2.018		
LS SE Diff. to Placebo [2]		4.4756		
95% CI [2]		-6.874, 10.910		
One-sided p-value [2]		0.3266		
Hedge's G (95% CI)		0.13 [-0.458, 0.713]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	77.8	-4.4	82.3	-7.3
SD	21.59	27.66	16.63	13.57
Median	75.0	0.0	83.3	0.0
Min, Max	33, 100	-67, 67	50, 100	-33, 17
LS Mean [2]		-5.758		-1.782
LS SE [2]		2.6234		3.3675
95% CI [2]		-10.973, -0.542		-8.479, 4.916
LS Mean Diff. to Placebo [2]		-3.976		
LS SE Diff. to Placebo [2]		4.1962		
95% CI [2]		-12.328, 4.376		
One-sided p-value [2]		0.8269		
Hedge's G (95% CI)		-0.28 [-0.887, 0.332]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	82.8	-2.1	81.0	-7.1
SD	18.69	19.74	19.46	14.19
Median	91.7	0.0	83.3	0.0
Min, Max	50, 100	-33, 50	50, 100	-50, 0
LS Mean [2]		-3.123		-2.671
LS SE [2]		2.3420		3.2175
95% CI [2]		-7.783, 1.537		-9.070, 3.728
LS Mean Diff. to Placebo [2]		-0.452		
LS SE Diff. to Placebo [2]		3.8882		
95% CI [2]		-8.194, 7.290		
One-sided p-value [2]		0.5461		
Hedge's G (95% CI)		-0.03 [-0.663, 0.594]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	76.9	-9.1	86.0	-4.4
SD	25.34	21.45	14.97	12.22
Median	83.3	0.0	83.3	0.0
Min, Max	0, 100	-67, 17	67, 100	-33, 17
LS Mean [2]		-7.597		-2.094
LS SE [2]		2.6539		3.3522
95% CI [2]		-12.874, -2.320		-8.758, 4.570
LS Mean Diff. to Placebo [2]		-5.503		
LS SE Diff. to Placebo [2]		4.1846		
95% CI [2]		-13.829, 2.823		
One-sided p-value [2]		0.9039		
Hedge's G (95% CI)		-0.37 [-0.950, 0.202]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	77.0	-4.6	85.9	-5.1
SD	24.97	21.77	19.06	17.19
Median	66.7	0.0	100.0	0.0
Min, Max	0, 100	-50, 50	50, 100	-50, 17
LS Mean [2]		-4.286		-0.688
LS SE [2]		2.6704		3.7002
95% CI [2]		-9.604, 1.033		-8.060, 6.684
LS Mean Diff. to Placebo [2]		-3.598		
LS SE Diff. to Placebo [2]		4.5110		
95% CI [2]		-12.591, 5.396		
One-sided p-value [2]		0.7861		
Hedge's G (95% CI)		-0.25 [-0.907, 0.406]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	79.4	-2.4	83.3	-6.1
SD	25.22	20.61	18.26	18.67
Median	100.0	0.0	83.3	0.0
Min, Max	33, 100	-33, 33	50, 100	-33, 33
LS Mean [2]		-6.694		-2.678
LS SE [2]		3.3794		4.5255
95% CI [2]		-13.486, 0.099		-11.774, 6.418
LS Mean Diff. to Placebo [2]		-4.016		
LS SE Diff. to Placebo [2]		5.6217		
95% CI [2]		-15.324, 7.292		
One-sided p-value [2]		0.7607		
Hedge's G (95% CI)		-0.26 [-0.988, 0.477]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	84.2	0.9	83.3	-13.3
SD	21.14	24.52	16.67	13.94
Median	100.0	0.0	83.3	-16.7
Min, Max	33, 100	-50, 50	67, 100	-33, 0
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	87.9	6.1	77.8	-11.1
SD	18.40	22.70	20.18	25.09
Median	100.0	0.0	75.0	0.0
Min, Max	50, 100	-50, 33	50, 100	-50, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	79.2	-8.3	70.8	-12.5
SD	20.26	20.72	28.46	36.96
Median	75.0	-8.3	75.0	0.0
Min, Max	50, 100	-33, 33	33, 100	-67, 17
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	81.9	2.8	66.7	-33.3
SD	18.06	24.45	23.57	23.57
Median	83.3	0.0	66.7	-33.3
Min, Max	50, 100	-33, 50	50, 83	-50, -17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	80.3	3.0	55.6	-33.3
SD	19.46	23.35	9.62	28.87
Median	83.3	0.0	50.0	-50.0
Min, Max	50, 100	-33, 50	50, 67	-50, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	87.5	2.1	66.7	-16.7
SD	14.77	5.89	27.22	33.33
Median	91.7	0.0	66.7	0.0
Min, Max	67, 100	0, 17	33, 100	-67, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	90.5	21.4	70.8	-16.7
SD	13.11	26.73	34.36	36.00
Median	100.0	16.7	75.0	-8.3
Min, Max	67, 100	-17, 67	33, 100	-67, 17
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	77.8	5.6	91.7	0.0
SD	20.18	29.19	11.79	23.57
Median	75.0	8.3	91.7	0.0
Min, Max	50, 100	-33, 50	83, 100	-17, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	76.7	6.7		
SD	19.00	30.28		
Median	83.3	0.0		
Min, Max	50, 100	-33, 50		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	0.0		
SD	NA	NA		
Median	100.0	0.0		
Min, Max	100, 100	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Cognitive Functioning Scale				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	0.0		
SD	NA	NA		
Median	100.0	0.0		
Min, Max	100, 100	0, 0		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	0.0		
SD	NA	NA		
Median	100.0	0.0		
Min, Max	100, 100	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Cognitive Functioning Scale				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	66.7	-16.7		
SD	NA	NA		
Median	66.7	-16.7		
Min, Max	67, 67	-17, -17		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	88.1	4.8	100.0	0.0
SD	31.50	8.13	NA	NA
Median	100.0	0.0	100.0	0.0
Min, Max	17, 100	0, 17	100, 100	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	68.6		70.7	
SD	28.31		27.43	
Median	66.7		66.7	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		7.478		-0.533
LS SE [2]		2.1066		2.2115
95% CI [2]		3.312, 11.643		-4.902, 3.835
LS Mean Diff. to Placebo [2]		8.011		
LS SE Diff. to Placebo [2]		2.8665		
95% CI [2]		2.345, 13.677		
One-sided p-value [2]		0.0030		
Hedge's G (95% CI)		0.45 [0.110, 0.793]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	71.7	2.5	75.2	3.8
SD	23.63	24.90	23.26	16.04
Median	66.7	0.0	66.7	0.0
Min, Max	0, 100	-50, 100	0, 100	-17, 50
LS Mean [2]		0.517		2.189
LS SE [2]		2.9198		3.0257
95% CI [2]		-5.273, 6.308		-3.810, 8.189
LS Mean Diff. to Placebo [2]		-1.672		
LS SE Diff. to Placebo [2]		4.0617		
95% CI [2]		-9.733, 6.389		
One-sided p-value [2]		0.6592		
Hedge's G (95% CI)		-0.08 [-0.447, 0.296]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	77.7	7.5	74.3	2.0
SD	22.87	20.56	26.86	14.54
Median	83.3	0.0	83.3	0.0
Min, Max	0, 100	-33, 50	0, 100	-33, 33
LS Mean [2]		5.480		2.000
LS SE [2]		2.4972		2.4150
95% CI [2]		0.535, 10.425		-2.785, 6.785
LS Mean Diff. to Placebo [2]		3.480		
LS SE Diff. to Placebo [2]		3.3076		
95% CI [2]		-3.076, 10.036		
One-sided p-value [2]		0.1475		
Hedge's G (95% CI)		0.19 [-0.182, 0.561]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	80.8	8.7	66.7	-4.2
SD	19.87	24.53	29.66	19.67
Median	83.3	0.0	66.7	0.0
Min, Max	33, 100	-33, 67	0, 100	-50, 50
LS Mean [2]		4.727		-4.163
LS SE [2]		3.0899		3.2902
95% CI [2]		-1.405, 10.860		-10.692, 2.366
LS Mean Diff. to Placebo [2]		8.890		
LS SE Diff. to Placebo [2]		4.3830		
95% CI [2]		0.185, 17.596		
One-sided p-value [2]		0.0227		
Hedge's G (95% CI)		0.44 [-0.006, 0.876]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	76.7	7.4	74.4	1.6
SD	19.97	28.01	27.16	24.10
Median	83.3	0.0	83.3	0.0
Min, Max	50, 100	-50, 100	0, 100	-67, 50
LS Mean [2]		2.782		-0.268
LS SE [2]		3.3066		3.3418
95% CI [2]		-3.775, 9.340		-6.896, 6.360
LS Mean Diff. to Placebo [2]		3.050		
LS SE Diff. to Placebo [2]		4.5739		
95% CI [2]		-6.028, 12.129		
One-sided p-value [2]		0.2532		
Hedge's G (95% CI)		0.14 [-0.287, 0.570]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	77.2	5.3	75.9	-1.4
SD	22.73	25.44	29.40	21.91
Median	83.3	0.0	83.3	0.0
Min, Max	0, 100	-67, 83	0, 100	-50, 33
LS Mean [2]		0.904		-0.447
LS SE [2]		3.4054		3.4998
95% CI [2]		-5.859, 7.668		-7.396, 6.501
LS Mean Diff. to Placebo [2]		1.352		
LS SE Diff. to Placebo [2]		4.7654		
95% CI [2]		-8.118, 10.821		
One-sided p-value [2]		0.3887		
Hedge's G (95% CI)		0.06 [-0.395, 0.524]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	75.6	6.2	72.1	-0.5
SD	31.57	31.08	26.66	18.03
Median	83.3	0.0	83.3	0.0
Min, Max	0, 100	-100, 100	0, 100	-33, 50
LS Mean [2]		0.756		0.092
LS SE [2]		3.5646		3.7496
95% CI [2]		-6.311, 7.823		-7.340, 7.525
LS Mean Diff. to Placebo [2]		0.664		
LS SE Diff. to Placebo [2]		5.0575		
95% CI [2]		-9.368, 10.696		
One-sided p-value [2]		0.4479		
Hedge's G (95% CI)		0.03 [-0.414, 0.472]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	77.9	8.9	71.1	-1.1
SD	24.32	22.81	27.31	16.02
Median	83.3	0.0	83.3	0.0
Min, Max	0, 100	-50, 83	0, 100	-33, 17
LS Mean [2]		6.066		1.485
LS SE [2]		2.6176		2.9073
95% CI [2]		0.874, 11.259		-4.280, 7.250
LS Mean Diff. to Placebo [2]		4.582		
LS SE Diff. to Placebo [2]		3.7710		
95% CI [2]		-2.903, 12.066		
One-sided p-value [2]		0.1137		
Hedge's G (95% CI)		0.28 [-0.197, 0.749]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	82.2	11.7	67.1	-3.4
SD	20.77	22.90	29.28	21.63
Median	83.3	0.0	66.7	0.0
Min, Max	33, 100	-33, 100	0, 100	-50, 33
LS Mean [2]		7.869		-3.492
LS SE [2]		2.7828		2.9963
95% CI [2]		2.353, 13.384		-9.430, 2.445
LS Mean Diff. to Placebo [2]		11.361		
LS SE Diff. to Placebo [2]		3.9384		
95% CI [2]		3.549, 19.173		
One-sided p-value [2]		0.0024		
Hedge's G (95% CI)		0.63 [0.172, 1.088]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	82.0	10.1	63.1	-9.5
SD	24.01	27.82	32.19	18.39
Median	100.0	0.0	66.7	0.0
Min, Max	17, 100	-50, 100	0, 100	-50, 33
LS Mean [2]		5.784		-6.722
LS SE [2]		3.3936		3.7329
95% CI [2]		-0.956, 12.523		-14.132, 0.689
LS Mean Diff. to Placebo [2]		12.505		
LS SE Diff. to Placebo [2]		4.9268		
95% CI [2]		2.714, 22.296		
One-sided p-value [2]		0.0065		
Hedge's G (95% CI)		0.61 [0.113, 1.111]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	84.3	13.2	68.6	-10.3
SD	21.30	29.81	33.44	21.12
Median	100.0	0.0	66.7	0.0
Min, Max	33, 100	-33, 100	0, 100	-67, 17
LS Mean [2]		10.620		-3.799
LS SE [2]		3.4014		3.7376
95% CI [2]		3.867, 17.374		-11.217, 3.618
LS Mean Diff. to Placebo [2]		14.420		
LS SE Diff. to Placebo [2]		4.9409		
95% CI [2]		4.603, 24.236		
One-sided p-value [2]		0.0022		
Hedge's G (95% CI)		0.74 [0.212, 1.267]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	76.8	7.6	79.2	-4.2
SD	31.16	33.62	25.18	20.41
Median	100.0	0.0	83.3	0.0
Min, Max	0, 100	-83, 100	0, 100	-50, 33
LS Mean [2]		4.397		-3.087
LS SE [2]		3.8916		4.4161
95% CI [2]		-3.334, 12.129		-11.855, 5.682
LS Mean Diff. to Placebo [2]		7.484		
LS SE Diff. to Placebo [2]		5.8295		
95% CI [2]		-4.102, 19.070		
One-sided p-value [2]		0.1013		
Hedge's G (95% CI)		0.34 [-0.190, 0.869]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	77.8	10.1	74.6	-6.8
SD	27.22	28.55	26.53	18.30
Median	83.3	0.0	83.3	0.0
Min, Max	17, 100	-33, 100	17, 100	-33, 33
LS Mean [2]		6.178		-3.795
LS SE [2]		3.0836		3.5633
95% CI [2]		0.058, 12.299		-10.861, 3.271
LS Mean Diff. to Placebo [2]		9.973		
LS SE Diff. to Placebo [2]		4.6158		
95% CI [2]		0.808, 19.138		
One-sided p-value [2]		0.0166		
Hedge's G (95% CI)		0.58 [0.026, 1.126]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	85.4	12.6	72.0	-2.4
SD	20.73	28.57	27.88	23.74
Median	100.0	0.0	66.7	0.0
Min, Max	33, 100	-33, 100	0, 100	-50, 33
LS Mean [2]		9.153		-0.177
LS SE [2]		3.0045		3.4887
95% CI [2]		3.189, 15.118		-7.100, 6.747
LS Mean Diff. to Placebo [2]		9.330		
LS SE Diff. to Placebo [2]		4.4781		
95% CI [2]		0.435, 18.225		
One-sided p-value [2]		0.0200		
Hedge's G (95% CI)		0.56 [-0.001, 1.113]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	84.9	16.7	64.5	-9.8
SD	20.35	27.22	34.20	23.94
Median	100.0	0.0	66.7	0.0
Min, Max	33, 100	-17, 100	0, 100	-50, 17
LS Mean [2]		11.192		-5.662
LS SE [2]		3.2467		3.6649
95% CI [2]		4.745, 17.640		-12.937, 1.613
LS Mean Diff. to Placebo [2]		16.854		
LS SE Diff. to Placebo [2]		4.7839		
95% CI [2]		7.348, 26.361		
One-sided p-value [2]		0.0003		
Hedge's G (95% CI)		0.95 [0.376, 1.527]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	81.9	11.8	70.8	-3.3
SD	20.25	27.69	25.29	20.66
Median	83.3	0.0	66.7	0.0
Min, Max	33, 100	-33, 100	17, 100	-33, 33
LS Mean [2]		6.897		-3.006
LS SE [2]		3.1394		3.7601
95% CI [2]		0.646, 13.147		-10.489, 4.477
LS Mean Diff. to Placebo [2]		9.902		
LS SE Diff. to Placebo [2]		4.7874		
95% CI [2]		0.366, 19.439		
One-sided p-value [2]		0.0210		
Hedge's G (95% CI)		0.56 [-0.005, 1.119]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	18 (25.0)	18 (25.0)
Mean	82.3	12.5	80.6	0.9
SD	20.71	27.44	27.56	17.59
Median	91.7	0.0	100.0	0.0
Min, Max	33, 100	-33, 100	0, 100	-33, 33
LS Mean [2]		9.075		3.800
LS SE [2]		2.6617		3.2535
95% CI [2]		3.790, 14.359		-2.660, 10.259
LS Mean Diff. to Placebo [2]		5.275		
LS SE Diff. to Placebo [2]		4.0902		
95% CI [2]		-2.851, 13.401		
One-sided p-value [2]		0.1002		
Hedge's G (95% CI)		0.36 [-0.221, 0.942]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	86.4	16.2	74.2	-5.3
SD	20.18	28.71	31.29	17.61
Median	100.0	16.7	83.3	0.0
Min, Max	33, 100	-33, 100	0, 100	-33, 33
LS Mean [2]		13.055		-1.980
LS SE [2]		2.9444		3.6068
95% CI [2]		7.208, 18.903		-9.141, 5.180
LS Mean Diff. to Placebo [2]		15.036		
LS SE Diff. to Placebo [2]		4.5456		
95% CI [2]		6.002, 24.069		
One-sided p-value [2]		0.0007		
Hedge's G (95% CI)		0.91 [0.321, 1.503]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	86.9	13.1	80.6	-2.0
SD	18.98	29.39	22.32	20.31
Median	100.0	0.0	83.3	0.0
Min, Max	33, 100	-33, 100	33, 100	-33, 33
LS Mean [2]		10.846		0.263
LS SE [2]		2.8200		3.6282
95% CI [2]		5.239, 16.453		-6.948, 7.475
LS Mean Diff. to Placebo [2]		10.583		
LS SE Diff. to Placebo [2]		4.4678		
95% CI [2]		1.695, 19.471		
One-sided p-value [2]		0.0101		
Hedge's G (95% CI)		0.67 [0.070, 1.270]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	80.6	10.6	77.1	-1.0
SD	20.57	32.60	22.67	21.49
Median	83.3	0.0	75.0	0.0
Min, Max	33, 100	-50, 100	33, 100	-33, 50
LS Mean [2]		5.045		-0.127
LS SE [2]		3.3066		4.2360
95% CI [2]		-1.548, 11.638		-8.575, 8.322
LS Mean Diff. to Placebo [2]		5.172		
LS SE Diff. to Placebo [2]		5.2861		
95% CI [2]		-5.381, 15.724		
One-sided p-value [2]		0.1657		
Hedge's G (95% CI)		0.29 [-0.323, 0.896]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	88.0	17.7	82.1	3.6
SD	19.04	29.61	17.86	20.86
Median	100.0	16.7	83.3	0.0
Min, Max	33, 100	-33, 100	50, 100	-33, 50
LS Mean [2]		15.531		5.254
LS SE [2]		2.6764		3.6516
95% CI [2]		10.202, 20.861		-2.015, 12.523
LS Mean Diff. to Placebo [2]		10.278		
LS SE Diff. to Placebo [2]		4.4198		
95% CI [2]		1.468, 19.087		
One-sided p-value [2]		0.0114		
Hedge's G (95% CI)		0.69 [0.043, 1.330]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	86.6	16.7	84.2	5.3
SD	18.96	28.87	22.55	27.25
Median	100.0	16.7	100.0	0.0
Min, Max	33, 100	-33, 100	33, 100	-33, 83
LS Mean [2]		12.310		5.639
LS SE [2]		2.8067		3.4743
95% CI [2]		6.714, 17.905		-1.290, 12.568
LS Mean Diff. to Placebo [2]		6.670		
LS SE Diff. to Placebo [2]		4.3661		
95% CI [2]		-2.046, 15.387		
One-sided p-value [2]		0.0657		
Hedge's G (95% CI)		0.43 [-0.145, 1.009]		

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	81.6	12.1	75.6	-7.7
SD	22.86	27.06	24.17	19.97
Median	83.3	0.0	66.7	0.0
Min, Max	0, 100	-33, 83	33, 100	-33, 17
LS Mean [2]		10.932		0.080
LS SE [2]		2.8533		3.9373
95% CI [2]		5.217, 16.646		-7.819, 7.979
LS Mean Diff. to Placebo [2]		10.852		
LS SE Diff. to Placebo [2]		4.7872		
95% CI [2]		1.241, 20.462		
One-sided p-value [2]		0.0138		
Hedge's G (95% CI)		0.71 [0.037, 1.380]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	86.5	15.1	77.3	0.0
SD	20.15	33.71	27.15	24.72
Median	100.0	16.7	83.3	0.0
Min, Max	33, 100	-33, 100	17, 100	-50, 33
LS Mean [2]		11.868		3.656
LS SE [2]		4.0477		5.4045
95% CI [2]		3.676, 20.061		-7.277, 14.590
LS Mean Diff. to Placebo [2]		8.212		
LS SE Diff. to Placebo [2]		6.6918		
95% CI [2]		-5.339, 21.763		
One-sided p-value [2]		0.1137		
Hedge's G (95% CI)		0.44 [-0.301, 1.174]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	82.5	12.3	53.3	-13.3
SD	25.14	33.72	36.13	32.06
Median	100.0	0.0	66.7	0.0
Min, Max	17, 100	-50, 83	0, 83	-67, 17
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	80.3	16.7	69.4	-8.3
SD	26.69	30.73	40.02	31.18
Median	83.3	0.0	83.3	0.0
Min, Max	17, 100	-17, 83	0, 100	-67, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 27				
n (%)	11 (15.7)	11 (15.7)	4 (5.6)	4 (5.6)
Mean	84.8	21.2	75.0	0.0
SD	20.35	27.98	28.87	13.61
Median	100.0	16.7	83.3	0.0
Min, Max	50, 100	-17, 83	33, 100	-17, 17
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	80.6	11.1	75.0	0.0
SD	22.29	24.96	35.36	0.00
Median	83.3	0.0	75.0	0.0
Min, Max	33, 100	-33, 67	50, 100	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	75.8	7.6	55.6	-16.7
SD	22.81	31.94	9.62	16.67
Median	66.7	0.0	50.0	-16.7
Min, Max	33, 100	-33, 67	50, 67	-33, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	89.6	27.1	66.7	16.7
SD	15.27	38.77	27.22	45.13
Median	100.0	16.7	66.7	0.0
Min, Max	67, 100	-17, 100	33, 100	-17, 83

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	78.6	14.3	75.0	-4.2
SD	15.85	36.55	16.67	20.97
Median	66.7	0.0	66.7	0.0
Min, Max	67, 100	-33, 83	67, 100	-33, 17
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	80.6	16.7	91.7	-8.3
SD	19.48	33.33	11.79	11.79
Median	83.3	0.0	91.7	-8.3
Min, Max	50, 100	0, 83	83, 100	-17, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	83.3	20.0		
SD	16.67	36.13		
Median	83.3	0.0		
Min, Max	67, 100	0, 83		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	0.0		
SD	NA	NA		
Median	100.0	0.0		
Min, Max	100, 100	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Social Functioning Scale				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	33.3		
SD	NA	NA		
Median	100.0	33.3		
Min, Max	100, 100	33, 33		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	100.0	33.3		
SD	NA	NA		
Median	100.0	33.3		
Min, Max	100, 100	33, 33		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Social Functioning Scale				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	50.0	-16.7		
SD	NA	NA		
Median	50.0	-16.7		
Min, Max	50, 50	-17, -17		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	69.0	2.4	33.3	0.0
SD	33.92	11.50	NA	NA
Median	66.7	0.0	33.3	0.0
Min, Max	0, 100	-17, 17	33, 33	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	40.2		40.8	
SD	27.82		29.53	
Median	33.3		44.4	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		-4.152		0.082
LS SE [2]		2.3211		2.4309
95% CI [2]		-8.743, 0.438		-4.721, 4.884
LS Mean Diff. to Placebo [2]		-4.234		
LS SE Diff. to Placebo [2]		3.1075		
95% CI [2]		-10.377, 1.909		
One-sided p-value [2]		0.9124		
Hedge's G (95% CI)		-0.22 [-0.555, 0.121]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	46.5	5.4	40.9	0.0
SD	29.04	28.09	26.13	25.28
Median	44.4	0.0	44.4	0.0
Min, Max	0, 100	-56, 89	0, 100	-89, 67
LS Mean [2]		6.027		0.855
LS SE [2]		3.2742		3.3834
95% CI [2]		-0.450, 12.503		-5.836, 7.547
LS Mean Diff. to Placebo [2]		5.171		
LS SE Diff. to Placebo [2]		4.5244		
95% CI [2]		-3.783, 14.126		
One-sided p-value [2]		0.1276		
Hedge's G (95% CI)		0.21 [-0.165, 0.580]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	40.3	0.2	42.2	3.2
SD	25.62	27.78	28.57	23.07
Median	33.3	0.0	44.4	0.0
Min, Max	0, 100	-67, 89	0, 100	-78, 78
LS Mean [2]		0.888		2.949
LS SE [2]		3.3114		3.2440
95% CI [2]		-5.663, 7.438		-3.471, 9.370
LS Mean Diff. to Placebo [2]		-2.062		
LS SE Diff. to Placebo [2]		4.4512		
95% CI [2]		-10.874, 6.751		
One-sided p-value [2]		0.6780		
Hedge's G (95% CI)		-0.08 [-0.455, 0.287]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	33.1	-1.0	36.9	-1.9
SD	24.62	24.88	24.71	23.53
Median	27.8	0.0	33.3	0.0
Min, Max	0, 89	-56, 89	0, 89	-56, 56
LS Mean [2]		-3.532		-1.070
LS SE [2]		3.3405		3.5003
95% CI [2]		-10.154, 3.089		-8.007, 5.868
LS Mean Diff. to Placebo [2]		-2.463		
LS SE Diff. to Placebo [2]		4.6650		
95% CI [2]		-11.717, 6.792		
One-sided p-value [2]		0.7006		
Hedge's G (95% CI)		-0.11 [-0.549, 0.324]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	38.5	-1.8	38.5	-1.4
SD	26.04	27.21	25.71	18.12
Median	33.3	0.0	44.4	0.0
Min, Max	0, 100	-56, 100	0, 100	-33, 56
LS Mean [2]		-0.972		-0.724
LS SE [2]		2.9675		2.9948
95% CI [2]		-6.847, 4.903		-6.654, 5.206
LS Mean Diff. to Placebo [2]		-0.248		
LS SE Diff. to Placebo [2]		4.0134		
95% CI [2]		-8.199, 7.704		
One-sided p-value [2]		0.5245		
Hedge's G (95% CI)		-0.01 [-0.441, 0.415]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	37.1	-0.3	35.8	-0.6
SD	26.25	24.44	27.36	21.38
Median	33.3	0.0	33.3	0.0
Min, Max	0, 89	-44, 89	0, 100	-56, 44
LS Mean [2]		0.611		-0.226
LS SE [2]		3.1651		3.2313
95% CI [2]		-5.661, 6.884		-6.627, 6.176
LS Mean Diff. to Placebo [2]		0.837		
LS SE Diff. to Placebo [2]		4.3328		
95% CI [2]		-7.755, 9.429		
One-sided p-value [2]		0.4236		
Hedge's G (95% CI)		0.04 [-0.416, 0.503]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	35.4	-3.6	32.4	-6.8
SD	27.57	25.51	21.18	19.75
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-56, 100	0, 67	-44, 33
LS Mean [2]		-3.724		-4.635
LS SE [2]		2.7696		2.8765
95% CI [2]		-9.206, 1.758		-10.328, 1.058
LS Mean Diff. to Placebo [2]		0.911		
LS SE Diff. to Placebo [2]		3.7780		
95% CI [2]		-6.572, 8.395		
One-sided p-value [2]		0.4049		
Hedge's G (95% CI)		0.05 [-0.392, 0.494]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 8				
n (%)	42 (60.0)	42 (60.0)	30 (41.7)	29 (40.3)
Mean	38.9	-3.2	43.0	1.1
SD	25.41	24.94	23.66	18.39
Median	33.3	0.0	44.4	11.1
Min, Max	0, 100	-67, 78	0, 89	-33, 33
LS Mean [2]		-4.047		0.926
LS SE [2]		2.9226		3.1750
95% CI [2]		-9.840, 1.746		-5.364, 7.217
LS Mean Diff. to Placebo [2]		-4.973		
LS SE Diff. to Placebo [2]		4.1115		
95% CI [2]		-13.127, 3.181		
One-sided p-value [2]		0.8854		
Hedge's G (95% CI)		-0.27 [-0.748, 0.202]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	32.4	-5.9	42.2	4.2
SD	25.02	26.88	25.82	22.06
Median	33.3	0.0	44.4	0.0
Min, Max	0, 100	-67, 78	0, 89	-56, 44
LS Mean [2]		-3.872		3.353
LS SE [2]		3.0576		3.2616
95% CI [2]		-9.926, 2.181		-3.102, 9.808
LS Mean Diff. to Placebo [2]		-7.225		
LS SE Diff. to Placebo [2]		4.2755		
95% CI [2]		-15.695, 1.244		
One-sided p-value [2]		0.9531		
Hedge's G (95% CI)		-0.37 [-0.817, 0.085]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	32.7	-2.9	45.6	7.1
SD	24.09	25.92	27.77	28.40
Median	33.3	0.0	44.4	5.6
Min, Max	0, 78	-67, 67	0, 100	-67, 89
LS Mean [2]		-4.276		4.039
LS SE [2]		3.2330		3.5037
95% CI [2]		-10.681, 2.129		-2.898, 10.977
LS Mean Diff. to Placebo [2]		-8.315		
LS SE Diff. to Placebo [2]		4.5878		
95% CI [2]		-17.410, 0.780		
One-sided p-value [2]		0.9636		
Hedge's G (95% CI)		-0.43 [-0.923, 0.064]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	30.1	-5.6	45.3	10.3
SD	21.63	22.10	26.47	16.61
Median	33.3	0.0	44.4	11.1
Min, Max	0, 78	-67, 33	0, 100	-22, 44
LS Mean [2]		-7.285		4.813
LS SE [2]		2.8323		3.0728
95% CI [2]		-12.904, -1.666		-1.278, 10.903
LS Mean Diff. to Placebo [2]		-12.097		
LS SE Diff. to Placebo [2]		3.9590		
95% CI [2]		-19.959, -4.236		
One-sided p-value [2]		0.9985		
Hedge's G (95% CI)		-0.75 [-1.277, -0.221]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Fatigue				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	36.4	-4.0	36.6	2.3
SD	29.17	29.37	27.51	17.94
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-67, 89	0, 100	-33, 33
LS Mean [2]		-1.650		-1.390
LS SE [2]		3.3561		3.6868
95% CI [2]		-8.303, 5.003		-8.693, 5.912
LS Mean Diff. to Placebo [2]		-0.260		
LS SE Diff. to Placebo [2]		4.8197		
95% CI [2]		-9.819, 9.299		
One-sided p-value [2]		0.5215		
Hedge's G (95% CI)		-0.01 [-0.540, 0.512]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Fatigue				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	37.4	-4.0	43.5	5.1
SD	28.03	27.75	25.49	21.06
Median	33.3	0.0	44.4	0.0
Min, Max	0, 100	-67, 78	0, 100	-33, 67
LS Mean [2]		-3.050		4.503
LS SE [2]		3.2527		3.6599
95% CI [2]		-9.504, 3.403		-2.749, 11.756
LS Mean Diff. to Placebo [2]		-7.553		
LS SE Diff. to Placebo [2]		4.7215		
95% CI [2]		-16.924, 1.817		
One-sided p-value [2]		0.9436		
Hedge's G (95% CI)		-0.42 [-0.962, 0.128]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Fatigue				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	26.9	-9.4	45.5	3.2
SD	22.57	22.59	26.32	18.31
Median	22.2	-11.1	44.4	0.0
Min, Max	0, 78	-67, 44	0, 100	-33, 44
LS Mean [2]		-6.290		4.484
LS SE [2]		3.1070		3.5495
95% CI [2]		-12.463, -0.116		-2.565, 11.533
LS Mean Diff. to Placebo [2]		-10.774		
LS SE Diff. to Placebo [2]		4.5443		
95% CI [2]		-19.810, -1.738		
One-sided p-value [2]		0.9900		
Hedge's G (95% CI)		-0.62 [-1.184, -0.065]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	30.1	-10.4	40.6	1.5
SD	24.04	23.99	30.26	23.08
Median	33.3	-11.1	33.3	0.0
Min, Max	0, 89	-67, 67	0, 100	-33, 56
LS Mean [2]		-6.653		-0.461
LS SE [2]		3.3488		3.7517
95% CI [2]		-13.301, -0.004		-7.905, 6.982
LS Mean Diff. to Placebo [2]		-6.191		
LS SE Diff. to Placebo [2]		4.8600		
95% CI [2]		-15.847, 3.465		
One-sided p-value [2]		0.8970		
Hedge's G (95% CI)		-0.34 [-0.890, 0.210]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	28.4	-6.2	43.3	3.9
SD	22.92	25.69	27.67	20.79
Median	22.2	-11.1	50.0	0.0
Min, Max	0, 78	-56, 78	0, 89	-44, 56
LS Mean [2]		-7.235		2.470
LS SE [2]		3.0035		3.5129
95% CI [2]		-13.191, -1.279		-4.492, 9.431
LS Mean Diff. to Placebo [2]		-9.705		
LS SE Diff. to Placebo [2]		4.4474		
95% CI [2]		-18.527, -0.882		
One-sided p-value [2]		0.9843		
Hedge's G (95% CI)		-0.58 [-1.138, -0.012]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	31.6	-8.0	39.2	4.7
SD	22.95	24.96	30.85	20.39
Median	33.3	-11.1	33.3	0.0
Min, Max	0, 78	-67, 78	0, 89	-56, 44
LS Mean [2]		-7.287		3.625
LS SE [2]		3.1985		3.7840
95% CI [2]		-13.638, -0.935		-3.887, 11.137
LS Mean Diff. to Placebo [2]		-10.912		
LS SE Diff. to Placebo [2]		4.7928		
95% CI [2]		-20.434, -1.389		
One-sided p-value [2]		0.9874		
Hedge's G (95% CI)		-0.62 [-1.203, -0.042]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Fatigue				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	30.0	-7.1	45.0	8.8
SD	26.42	28.44	34.85	23.59
Median	33.3	0.0	44.4	0.0
Min, Max	0, 89	-56, 89	0, 100	-33, 67
LS Mean [2]		-5.994		1.077
LS SE [2]		3.4692		4.1638
95% CI [2]		-12.875, 0.887		-7.176, 9.331
LS Mean Diff. to Placebo [2]		-7.071		
LS SE Diff. to Placebo [2]		5.2594		
95% CI [2]		-17.507, 3.365		
One-sided p-value [2]		0.9091		
Hedge's G (95% CI)		-0.37 [-0.935, 0.203]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	29.6	-5.7	34.0	1.3
SD	21.09	26.37	24.54	23.53
Median	33.3	0.0	33.3	0.0
Min, Max	0, 67	-67, 67	0, 89	-33, 56
LS Mean [2]		-5.606		-5.620
LS SE [2]		3.0423		3.8027
95% CI [2]		-11.643, 0.432		-13.161, 1.921
LS Mean Diff. to Placebo [2]		0.014		
LS SE Diff. to Placebo [2]		4.6800		
95% CI [2]		-9.276, 9.305		
One-sided p-value [2]		0.4988		
Hedge's G (95% CI)		0.00 [-0.584, 0.586]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Fatigue				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	33.3	-5.9	34.7	-1.4
SD	24.06	30.43	24.64	26.25
Median	33.3	0.0	33.3	0.0
Min, Max	0, 89	-67, 78	0, 78	-56, 44
LS Mean [2]		-4.229		-6.852
LS SE [2]		3.2879		4.1064
95% CI [2]		-10.757, 2.298		-15.003, 1.299
LS Mean Diff. to Placebo [2]		2.623		
LS SE Diff. to Placebo [2]		5.1078		
95% CI [2]		-7.526, 12.771		
One-sided p-value [2]		0.3044		
Hedge's G (95% CI)		0.15 [-0.460, 0.755]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	28.8	-10.4	44.4	7.1
SD	19.11	22.74	29.24	27.08
Median	27.8	-11.1	44.4	11.1
Min, Max	0, 67	-67, 56	0, 89	-56, 56
LS Mean [2]		-9.520		1.389
LS SE [2]		2.7526		3.6314
95% CI [2]		-14.982, -4.057		-5.811, 8.589
LS Mean Diff. to Placebo [2]		-10.908		
LS SE Diff. to Placebo [2]		4.3794		
95% CI [2]		-19.603, -2.214		
One-sided p-value [2]		0.9928		
Hedge's G (95% CI)		-0.71 [-1.359, -0.069]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Fatigue				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	29.4	-10.0	35.7	0.0
SD	21.57	26.66	26.08	27.72
Median	33.3	-11.1	33.3	0.0
Min, Max	0, 78	-67, 67	0, 100	-67, 67
LS Mean [2]		-8.380		-1.817
LS SE [2]		2.9658		3.6179
95% CI [2]		-14.266, -2.494		-8.993, 5.359
LS Mean Diff. to Placebo [2]		-6.563		
LS SE Diff. to Placebo [2]		4.5163		
95% CI [2]		-15.530, 2.405		
One-sided p-value [2]		0.9252		
Hedge's G (95% CI)		-0.40 [-0.981, 0.172]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	34.9	-7.3	37.6	6.8
SD	26.01	26.44	27.42	22.47
Median	33.3	-11.1	44.4	0.0
Min, Max	0, 100	-67, 56	0, 100	-22, 67
LS Mean [2]		-6.734		-3.493
LS SE [2]		3.2702		4.3974
95% CI [2]		-13.236, -0.231		-12.238, 5.252
LS Mean Diff. to Placebo [2]		-3.240		
LS SE Diff. to Placebo [2]		5.3688		
95% CI [2]		-13.926, 7.445		
One-sided p-value [2]		0.7261		
Hedge's G (95% CI)		-0.19 [-0.841, 0.470]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Fatigue				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	30.7	-0.5	33.3	4.0
SD	25.56	27.10	28.11	22.92
Median	33.3	0.0	33.3	0.0
Min, Max	0, 78	-44, 78	0, 78	-44, 44
LS Mean [2]		-2.697		-6.312
LS SE [2]		3.6057		4.7228
95% CI [2]		-9.904, 4.510		-15.753, 3.129
LS Mean Diff. to Placebo [2]		3.615		
LS SE Diff. to Placebo [2]		5.7244		
95% CI [2]		-7.836, 15.066		
One-sided p-value [2]		0.2650		
Hedge's G (95% CI)		0.22 [-0.514, 0.948]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	25.7	-5.3	48.9	13.3
SD	26.20	25.76	25.58	16.48
Median	22.2	-11.1	55.6	11.1
Min, Max	0, 78	-44, 67	22, 78	-11, 33
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	24.2	-11.1	48.1	9.3
SD	16.34	15.71	34.19	23.74
Median	22.2	-11.1	38.9	0.0
Min, Max	11, 67	-44, 11	11, 100	-11, 44

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 27				
n (%)	11 (15.7)	11 (15.7)	4 (5.6)	4 (5.6)
Mean	31.3	-7.1	50.0	13.9
SD	28.03	30.74	37.95	37.82
Median	22.2	-11.1	44.4	5.6
Min, Max	0, 78	-44, 67	11, 100	-22, 67
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	31.5	-13.0	55.6	38.9
SD	23.61	15.59	62.85	39.28
Median	33.3	-11.1	55.6	38.9
Min, Max	0, 67	-33, 11	11, 100	11, 67

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	35.4	-9.1	48.1	18.5
SD	25.25	37.78	33.95	23.13
Median	33.3	-11.1	55.6	11.1
Min, Max	0, 89	-67, 89	11, 78	0, 44
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	26.4	-16.7	58.3	0.0
SD	15.64	35.63	36.71	59.49
Median	22.2	-22.2	61.1	5.6
Min, Max	0, 56	-67, 56	11, 100	-78, 67

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	31.7	-20.6	38.9	13.9
SD	13.50	19.70	33.33	21.03
Median	22.2	-22.2	33.3	5.6
Min, Max	22, 56	-56, 0	11, 78	0, 44
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	42.6	-9.3	16.7	11.1
SD	17.80	40.01	7.86	15.71
Median	44.4	-22.2	16.7	11.1
Min, Max	22, 67	-44, 67	11, 22	0, 22

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	28.9	-28.9		
SD	25.58	27.89		
Median	22.2	-22.2		
Min, Max	0, 56	-78, -11		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-22.2		
SD	NA	NA		
Median	0.0	-22.2		
Min, Max	0, 0	-22, -22		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Fatigue				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-22.2		
SD	NA	NA		
Median	0.0	-22.2		
Min, Max	0, 0	-22, -22		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-22.2		
SD	NA	NA		
Median	0.0	-22.2		
Min, Max	0, 0	-22, -22		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Fatigue				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	55.6	11.1		
SD	NA	NA		
Median	55.6	11.1		
Min, Max	56, 56	11, 11		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	34.9	-9.5	33.3	0.0
SD	33.60	13.50	NA	NA
Median	22.2	-11.1	33.3	0.0
Min, Max	0, 100	-33, 11	33, 33	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	6.9		8.8	
SD	13.46		15.73	
Median	0.0		0.0	
Min, Max	0, 67		0, 83	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		2.926		-2.025
LS SE [2]		1.2597		1.3259
95% CI [2]		0.435, 5.418		-4.644, 0.595
LS Mean Diff. to Placebo [2]		4.951		
LS SE Diff. to Placebo [2]		1.7121		
95% CI [2]		1.565, 8.337		
One-sided p-value [2]		0.0022		
Hedge's G (95% CI)		0.47 [0.124, 0.808]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	19.2	13.3	10.1	0.3
SD	18.37	18.61	16.45	14.57
Median	16.7	16.7	0.0	0.0
Min, Max	0, 67	-33, 50	0, 67	-33, 50
LS Mean [2]		12.679		1.735
LS SE [2]		2.3163		2.4245
95% CI [2]		8.089, 17.269		-3.069, 6.539
LS Mean Diff. to Placebo [2]		10.944		
LS SE Diff. to Placebo [2]		3.2981		
95% CI [2]		4.406, 17.482		
One-sided p-value [2]		0.0006		
Hedge's G (95% CI)		0.62 [0.237, 0.997]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	14.8	9.1	7.1	-1.1
SD	16.23	15.18	14.91	15.74
Median	16.7	0.0	0.0	0.0
Min, Max	0, 50	-17, 50	0, 67	-50, 67
LS Mean [2]		7.124		-0.197
LS SE [2]		2.3199		2.2513
95% CI [2]		2.526, 11.722		-4.661, 4.267
LS Mean Diff. to Placebo [2]		7.321		
LS SE Diff. to Placebo [2]		3.1734		
95% CI [2]		1.027, 13.616		
One-sided p-value [2]		0.0115		
Hedge's G (95% CI)		0.43 [0.053, 0.803]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	10.1	4.7	3.2	-6.5
SD	15.10	16.73	8.64	13.96
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-33, 50	0, 33	-50, 17
LS Mean [2]		4.560		-3.919
LS SE [2]		1.9759		2.1188
95% CI [2]		0.638, 8.482		-8.125, 0.286
LS Mean Diff. to Placebo [2]		8.479		
LS SE Diff. to Placebo [2]		2.8376		
95% CI [2]		2.843, 14.116		
One-sided p-value [2]		0.0018		
Hedge's G (95% CI)		0.65 [0.200, 1.094]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	10.9	5.4	2.8	-5.3
SD	19.55	19.15	8.25	13.14
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-17, 100	0, 33	-50, 17
LS Mean [2]		3.290		-3.771
LS SE [2]		2.2167		2.2490
95% CI [2]		-1.107, 7.687		-8.233, 0.690
LS Mean Diff. to Placebo [2]		7.062		
LS SE Diff. to Placebo [2]		3.0967		
95% CI [2]		0.915, 13.208		
One-sided p-value [2]		0.0124		
Hedge's G (95% CI)		0.49 [0.054, 0.922]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	11.8	6.6	5.1	-4.3
SD	20.10	16.68	9.61	15.31
Median	0.0	0.0	0.0	0.0
Min, Max	0, 83	-17, 67	0, 33	-50, 17
LS Mean [2]		6.719		-2.751
LS SE [2]		2.1933		2.2545
95% CI [2]		2.368, 11.071		-7.222, 1.721
LS Mean Diff. to Placebo [2]		9.470		
LS SE Diff. to Placebo [2]		3.0857		
95% CI [2]		3.345, 15.595		
One-sided p-value [2]		0.0014		
Hedge's G (95% CI)		0.70 [0.232, 1.178]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	10.9	5.0	3.6	-5.6
SD	17.40	16.07	9.73	13.21
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-33, 50	0, 33	-50, 17
LS Mean [2]		3.685		-3.317
LS SE [2]		1.9504		2.0655
95% CI [2]		-0.182, 7.553		-7.413, 0.779
LS Mean Diff. to Placebo [2]		7.002		
LS SE Diff. to Placebo [2]		2.7706		
95% CI [2]		1.503, 12.501		
One-sided p-value [2]		0.0066		
Hedge's G (95% CI)		0.56 [0.104, 1.006]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	8.1	0.8	7.2	-4.0
SD	13.30	10.26	13.62	18.18
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-17, 33	0, 50	-50, 33
LS Mean [2]		0.665		-2.063
LS SE [2]		1.6051		1.8214
95% CI [2]		-2.519, 3.849		-5.675, 1.549
LS Mean Diff. to Placebo [2]		2.728		
LS SE Diff. to Placebo [2]		2.3442		
95% CI [2]		-1.925, 7.381		
One-sided p-value [2]		0.1237		
Hedge's G (95% CI)		0.27 [-0.207, 0.739]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	8.3	3.0	4.8	-6.4
SD	14.15	15.36	11.12	14.80
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-17, 67	0, 50	-50, 17
LS Mean [2]		2.913		-2.825
LS SE [2]		1.7700		1.9372
95% CI [2]		-0.599, 6.425		-6.667, 1.017
LS Mean Diff. to Placebo [2]		5.738		
LS SE Diff. to Placebo [2]		2.5533		
95% CI [2]		0.667, 10.808		
One-sided p-value [2]		0.0135		
Hedge's G (95% CI)		0.50 [0.043, 0.951]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	5.7	1.8	4.8	-6.0
SD	9.71	10.81	10.00	16.49
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-17, 33	0, 33	-50, 17
LS Mean [2]		1.362		-2.794
LS SE [2]		1.5119		1.6752
95% CI [2]		-1.640, 4.364		-6.119, 0.532
LS Mean Diff. to Placebo [2]		4.156		
LS SE Diff. to Placebo [2]		2.1849		
95% CI [2]		-0.188, 8.499		
One-sided p-value [2]		0.0303		
Hedge's G (95% CI)		0.46 [-0.039, 0.949]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	5.4	-1.5	4.5	-2.6
SD	11.40	11.14	12.07	13.07
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-17, 33	0, 50	-33, 33
LS Mean [2]		-0.043		-2.891
LS SE [2]		1.5838		1.7554
95% CI [2]		-3.190, 3.104		-6.377, 0.595
LS Mean Diff. to Placebo [2]		2.847		
LS SE Diff. to Placebo [2]		2.2688		
95% CI [2]		-1.666, 7.361		
One-sided p-value [2]		0.1065		
Hedge's G (95% CI)		0.31 [-0.201, 0.826]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	11.1	4.5	2.8	-2.8
SD	17.01	13.35	8.03	9.41
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-17, 50	0, 33	-33, 17
LS Mean [2]		4.611		-3.702
LS SE [2]		1.8726		2.1164
95% CI [2]		0.883, 8.340		-7.914, 0.510
LS Mean Diff. to Placebo [2]		8.313		
LS SE Diff. to Placebo [2]		2.7465		
95% CI [2]		2.839, 13.787		
One-sided p-value [2]		0.0017		
Hedge's G (95% CI)		0.78 [0.239, 1.330]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	10.1	2.0	1.4	-3.8
SD	18.61	13.67	4.80	11.42
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-33, 33	0, 17	-50, 0
LS Mean [2]		3.262		-5.334
LS SE [2]		1.8696		2.1894
95% CI [2]		-0.463, 6.986		-9.693, -0.976
LS Mean Diff. to Placebo [2]		8.596		
LS SE Diff. to Placebo [2]		2.8091		
95% CI [2]		2.996, 14.196		
One-sided p-value [2]		0.0016		
Hedge's G (95% CI)		0.81 [0.254, 1.375]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	5.6	0.0	10.6	-2.4
SD	11.54	10.21	20.28	23.74
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-33, 17	0, 67	-50, 50
LS Mean [2]		2.209		0.994
LS SE [2]		2.4594		2.9452
95% CI [2]		-2.700, 7.117		-4.881, 6.870
LS Mean Diff. to Placebo [2]		1.214		
LS SE Diff. to Placebo [2]		3.8011		
95% CI [2]		-6.376, 8.804		
One-sided p-value [2]		0.3752		
Hedge's G (95% CI)		0.09 [-0.460, 0.635]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	7.5	0.5	10.9	-2.3
SD	12.05	10.96	22.81	28.31
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-33, 17	0, 100	-50, 100
LS Mean [2]		1.121		-0.053
LS SE [2]		2.5506		2.9689
95% CI [2]		-3.959, 6.200		-5.964, 5.858
LS Mean Diff. to Placebo [2]		1.174		
LS SE Diff. to Placebo [2]		3.8640		
95% CI [2]		-6.526, 8.874		
One-sided p-value [2]		0.3811		
Hedge's G (95% CI)		0.08 [-0.463, 0.630]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	8.8	2.9	10.0	-0.8
SD	15.48	13.28	20.52	26.20
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-33, 33	0, 83	-50, 83
LS Mean [2]		2.886		1.183
LS SE [2]		2.4371		2.9967
95% CI [2]		-1.966, 7.739		-4.781, 7.147
LS Mean Diff. to Placebo [2]		1.703		
LS SE Diff. to Placebo [2]		3.8209		
95% CI [2]		-5.907, 9.313		
One-sided p-value [2]		0.3285		
Hedge's G (95% CI)		0.12 [-0.430, 0.675]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	9.9	3.6	6.1	-3.5
SD	15.18	12.51	11.40	18.07
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-17, 50	0, 33	-50, 33
LS Mean [2]		3.583		-0.135
LS SE [2]		2.0336		2.4835
95% CI [2]		-0.473, 7.638		-5.088, 4.817
LS Mean Diff. to Placebo [2]		3.718		
LS SE Diff. to Placebo [2]		3.1541		
95% CI [2]		-2.576, 10.012		
One-sided p-value [2]		0.1213		
Hedge's G (95% CI)		0.33 [-0.241, 0.901]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	7.1	0.5	8.3	-2.6
SD	17.69	14.12	19.12	17.80
Median	0.0	0.0	0.0	0.0
Min, Max	0, 83	-33, 50	0, 67	-33, 50
LS Mean [2]		2.118		-1.826
LS SE [2]		2.3571		2.9188
95% CI [2]		-2.581, 6.818		-7.644, 3.992
LS Mean Diff. to Placebo [2]		3.945		
LS SE Diff. to Placebo [2]		3.6974		
95% CI [2]		-3.432, 11.321		
One-sided p-value [2]		0.1449		
Hedge's G (95% CI)		0.30 [-0.270, 0.865]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	8.1	3.0	7.4	-2.9
SD	13.26	12.81	16.39	17.91
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-33, 50	0, 50	-50, 33
LS Mean [2]		2.583		-1.200
LS SE [2]		1.8839		2.4173
95% CI [2]		-1.171, 6.337		-6.015, 3.615
LS Mean Diff. to Placebo [2]		3.783		
LS SE Diff. to Placebo [2]		3.0069		
95% CI [2]		-2.212, 9.778		
One-sided p-value [2]		0.1062		
Hedge's G (95% CI)		0.36 [-0.231, 0.948]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	6.7	1.7	7.3	-1.0
SD	12.07	14.75	17.18	19.69
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-33, 50	0, 50	-50, 33
LS Mean [2]		0.648		-0.115
LS SE [2]		2.0902		2.6832
95% CI [2]		-3.517, 4.813		-5.462, 5.232
LS Mean Diff. to Placebo [2]		0.763		
LS SE Diff. to Placebo [2]		3.3520		
95% CI [2]		-5.922, 7.448		
One-sided p-value [2]		0.4103		
Hedge's G (95% CI)		0.07 [-0.540, 0.674]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	6.3	0.0	4.8	-3.6
SD	11.00	10.37	12.10	13.36
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-33, 17	0, 33	-33, 17
LS Mean [2]		0.746		-3.779
LS SE [2]		1.4714		2.0330
95% CI [2]		-2.187, 3.680		-7.830, 0.272
LS Mean Diff. to Placebo [2]		4.526		
LS SE Diff. to Placebo [2]		2.4283		
95% CI [2]		-0.321, 9.372		
One-sided p-value [2]		0.0334		
Hedge's G (95% CI)		0.55 [-0.090, 1.186]		

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	4.3	-0.5	7.0	-0.9
SD	8.57	10.08	12.81	18.82
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 17	0, 33	-50, 33
LS Mean [2]		0.206		-0.856
LS SE [2]		1.7618		2.1577
95% CI [2]		-3.308, 3.721		-5.159, 3.446
LS Mean Diff. to Placebo [2]		1.063		
LS SE Diff. to Placebo [2]		2.7215		
95% CI [2]		-4.371, 6.496		
One-sided p-value [2]		0.3487		
Hedge's G (95% CI)		0.11 [-0.461, 0.681]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	6.9	-1.1	2.6	-9.0
SD	13.74	7.63	9.25	17.50
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-17, 17	0, 33	-50, 17
LS Mean [2]		-0.089		-5.522
LS SE [2]		1.3869		1.9198
95% CI [2]		-2.853, 2.674		-9.349, -1.695
LS Mean Diff. to Placebo [2]		5.433		
LS SE Diff. to Placebo [2]		2.2793		
95% CI [2]		0.883, 9.983		
One-sided p-value [2]		0.0100		
Hedge's G (95% CI)		0.73 [0.057, 1.402]		

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	5.6	-0.8	1.5	-10.6
SD	12.17	11.15	5.03	17.12
Median	0.0	0.0	0.0	0.0
Min, Max	0, 50	-33, 17	0, 17	-50, 0
LS Mean [2]		0.463		-3.434
LS SE [2]		1.7304		2.3607
95% CI [2]		-3.029, 3.954		-8.194, 1.326
LS Mean Diff. to Placebo [2]		3.897		
LS SE Diff. to Placebo [2]		2.8723		
95% CI [2]		-1.905, 9.698		
One-sided p-value [2]		0.0912		
Hedge's G (95% CI)		0.48 [-0.258, 1.220]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	1.8	-2.6	0.0	-16.7
SD	5.26	11.47	0.00	20.41
Median	0.0	0.0	0.0	-16.7
Min, Max	0, 17	-33, 17	0, 0	-50, 0
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	1.5	-3.0	5.6	-2.8
SD	5.03	12.51	13.61	12.55
Median	0.0	0.0	0.0	0.0
Min, Max	0, 17	-33, 17	0, 33	-17, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 27				
n (%)	11 (15.7)	11 (15.7)	4 (5.6)	4 (5.6)
Mean	1.5	-1.5	12.5	4.2
SD	5.03	11.68	15.96	15.96
Median	0.0	0.0	8.3	8.3
Min, Max	0, 17	-33, 17	0, 33	-17, 17
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	4.2	-2.8	0.0	-8.3
SD	7.54	9.62	0.00	11.79
Median	0.0	0.0	0.0	-8.3
Min, Max	0, 17	-17, 17	0, 0	-17, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	1.5	-4.5	5.6	-5.6
SD	5.03	10.78	9.62	9.62
Median	0.0	0.0	0.0	0.0
Min, Max	0, 17	-33, 0	0, 17	-17, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	2.1	-4.2	12.5	0.0
SD	5.89	7.72	15.96	13.61
Median	0.0	0.0	8.3	0.0
Min, Max	0, 17	-17, 0	0, 33	-17, 17

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	2.4	-9.5	0.0	-8.3
SD	6.30	13.11	0.00	9.62
Median	0.0	0.0	0.0	-8.3
Min, Max	0, 17	-33, 0	0, 0	-17, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	0.0	-11.1	0.0	0.0
SD	0.00	13.61	0.00	0.00
Median	0.0	-8.3	0.0	0.0
Min, Max	0, 0	-33, 0	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Nausea and Vomiting				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	3.3	-6.7		
SD	7.45	9.13		
Median	0.0	0.0		
Min, Max	0, 17	-17, 0		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Nausea and Vomiting				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	16.7	0.0		
SD	NA	NA		
Median	16.7	0.0		
Min, Max	17, 17	0, 0		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	9.5	2.4	0.0	-50.0
SD	18.90	11.50	NA	NA
Median	0.0	0.0	0.0	-50.0
Min, Max	0, 50	-17, 17	0, 0	-50, -50

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	13.8		15.2	
SD	24.40		24.53	
Median	0.0		0.0	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		0.652		0.294
LS SE [2]		1.8040		1.8950
95% CI [2]		-2.919, 4.223		-3.452, 4.041
LS Mean Diff. to Placebo [2]		0.358		
LS SE Diff. to Placebo [2]		2.4443		
95% CI [2]		-4.479, 5.194		
One-sided p-value [2]		0.4420		
Hedge's G (95% CI)		0.02 [-0.314, 0.361]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	21.1	8.3	15.1	-2.6
SD	30.67	27.19	24.95	19.63
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 100	-33, 33
LS Mean [2]		8.313		-1.669
LS SE [2]		3.0663		3.2229
95% CI [2]		2.243, 14.384		-8.049, 4.711
LS Mean Diff. to Placebo [2]		9.982		
LS SE Diff. to Placebo [2]		4.3491		
95% CI [2]		1.368, 18.597		
One-sided p-value [2]		0.0118		
Hedge's G (95% CI)		0.42 [0.049, 0.800]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 3				
n (%)	52 (74.3)	52 (74.3)	59 (81.9)	59 (81.9)
Mean	10.9	-1.9	15.8	0.6
SD	19.49	22.30	26.52	23.56
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 100	-33, 100
LS Mean [2]		-0.890		1.608
LS SE [2]		2.7912		2.6905
95% CI [2]		-6.413, 4.633		-3.718, 6.934
LS Mean Diff. to Placebo [2]		-2.499		
LS SE Diff. to Placebo [2]		3.7606		
95% CI [2]		-9.946, 4.949		
One-sided p-value [2]		0.7461		
Hedge's G (95% CI)		-0.12 [-0.496, 0.251]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	13.0	1.4	15.3	-1.9
SD	19.22	21.03	23.03	19.43
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 33	0, 67	-33, 33
LS Mean [2]		1.803		-1.013
LS SE [2]		2.5112		2.7032
95% CI [2]		-3.179, 6.784		-6.375, 4.350
LS Mean Diff. to Placebo [2]		2.815		
LS SE Diff. to Placebo [2]		3.5769		
95% CI [2]		-4.285, 9.916		
One-sided p-value [2]		0.2166		
Hedge's G (95% CI)		0.17 [-0.268, 0.606]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	13.2	-1.6	19.5	3.3
SD	23.16	19.18	27.86	17.96
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-33, 67	0, 100	-33, 33
LS Mean [2]		1.252		3.590
LS SE [2]		2.5515		2.5896
95% CI [2]		-3.806, 6.310		-1.545, 8.724
LS Mean Diff. to Placebo [2]		-2.338		
LS SE Diff. to Placebo [2]		3.5091		
95% CI [2]		-9.300, 4.625		
One-sided p-value [2]		0.7466		
Hedge's G (95% CI)		-0.14 [-0.569, 0.288]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	35 (48.6)	34 (47.2)
Mean	14.0	0.0	14.3	0.0
SD	24.05	24.51	23.27	14.21
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 67	0, 67	-33, 33
LS Mean [2]		2.790		0.308
LS SE [2]		2.7778		2.8855
95% CI [2]		-2.726, 8.306		-5.419, 6.035
LS Mean Diff. to Placebo [2]		2.482		
LS SE Diff. to Placebo [2]		3.8904		
95% CI [2]		-5.247, 10.211		
One-sided p-value [2]		0.2626		
Hedge's G (95% CI)		0.15 [-0.317, 0.609]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	19.4	4.7	17.1	-1.9
SD	31.06	28.71	26.78	17.72
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 100	-33, 33
LS Mean [2]		8.351		-0.302
LS SE [2]		3.6769		3.9298
95% CI [2]		1.048, 15.655		-8.107, 7.502
LS Mean Diff. to Placebo [2]		8.654		
LS SE Diff. to Placebo [2]		5.2804		
95% CI [2]		-1.841, 19.148		
One-sided p-value [2]		0.0524		
Hedge's G (95% CI)		0.36 [-0.084, 0.809]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	11.6	-3.9	18.9	0.0
SD	20.42	26.44	29.92	19.92
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 100	-33, 33
LS Mean [2]		-0.564		1.923
LS SE [2]		2.8974		3.2905
95% CI [2]		-6.315, 5.187		-4.605, 8.452
LS Mean Diff. to Placebo [2]		-2.488		
LS SE Diff. to Placebo [2]		4.2682		
95% CI [2]		-10.963, 5.988		
One-sided p-value [2]		0.7193		
Hedge's G (95% CI)		-0.13 [-0.606, 0.337]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	11.4	-1.5	17.1	2.0
SD	15.98	22.68	29.56	18.24
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 100	-33, 33
LS Mean [2]		1.785		2.230
LS SE [2]		2.7470		2.9929
95% CI [2]		-3.667, 7.237		-3.708, 8.169
LS Mean Diff. to Placebo [2]		-0.445		
LS SE Diff. to Placebo [2]		3.9463		
95% CI [2]		-8.283, 7.393		
One-sided p-value [2]		0.5448		
Hedge's G (95% CI)		-0.02 [-0.472, 0.423]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	9.6	-2.6	19.0	4.8
SD	17.17	24.97	27.86	17.48
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 100	-33, 33
LS Mean [2]		-2.022		3.117
LS SE [2]		2.6603		2.9490
95% CI [2]		-7.303, 3.260		-2.736, 8.970
LS Mean Diff. to Placebo [2]		-5.138		
LS SE Diff. to Placebo [2]		3.8552		
95% CI [2]		-12.799, 2.522		
One-sided p-value [2]		0.9070		
Hedge's G (95% CI)		-0.32 [-0.811, 0.171]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	9.8	-3.9	11.5	3.8
SD	19.30	28.15	22.98	10.86
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 67	0, 33
LS Mean [2]		-0.748		-1.583
LS SE [2]		2.9895		3.3226
95% CI [2]		-6.700, 5.204		-8.195, 5.028
LS Mean Diff. to Placebo [2]		0.835		
LS SE Diff. to Placebo [2]		4.3636		
95% CI [2]		-7.861, 9.531		
One-sided p-value [2]		0.4244		
Hedge's G (95% CI)		0.05 [-0.462, 0.559]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	13.1	1.0	12.5	5.6
SD	18.52	28.24	27.47	16.05
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 100	0, 67
LS Mean [2]		0.899		0.251
LS SE [2]		3.1021		3.5226
95% CI [2]		-5.266, 7.064		-6.747, 7.249
LS Mean Diff. to Placebo [2]		0.647		
LS SE Diff. to Placebo [2]		4.5853		
95% CI [2]		-8.471, 9.766		
One-sided p-value [2]		0.4440		
Hedge's G (95% CI)		0.04 [-0.489, 0.563]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Dyspnoea				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	16.2	0.0	15.9	9.1
SD	18.86	30.05	22.18	18.35
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 67	-33, 33
LS Mean [2]		4.519		4.924
LS SE [2]		3.2830		3.8188
95% CI [2]		-2.024, 11.062		-2.681, 12.529
LS Mean Diff. to Placebo [2]		-0.405		
LS SE Diff. to Placebo [2]		4.9655		
95% CI [2]		-10.306, 9.496		
One-sided p-value [2]		0.5324		
Hedge's G (95% CI)		-0.02 [-0.561, 0.518]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	8.1	-1.0	19.7	4.8
SD	16.73	15.56	28.47	28.45
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-33, 33	0, 100	-67, 67
LS Mean [2]		-0.068		4.304
LS SE [2]		2.9124		3.4112
95% CI [2]		-5.864, 5.727		-2.483, 11.090
LS Mean Diff. to Placebo [2]		-4.372		
LS SE Diff. to Placebo [2]		4.3979		
95% CI [2]		-13.129, 4.386		
One-sided p-value [2]		0.8383		
Hedge's G (95% CI)		-0.27 [-0.817, 0.282]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Dyspnoea				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	10.8	-2.2	13.0	-1.5
SD	18.03	22.67	21.88	26.18
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 67	-67, 67
LS Mean [2]		1.159		-0.260
LS SE [2]		2.9135		3.3304
95% CI [2]		-4.642, 6.960		-6.889, 6.369
LS Mean Diff. to Placebo [2]		1.419		
LS SE Diff. to Placebo [2]		4.3216		
95% CI [2]		-7.193, 10.032		
One-sided p-value [2]		0.3718		
Hedge's G (95% CI)		0.09 [-0.458, 0.635]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	12.7	0.0	15.0	1.7
SD	20.13	23.21	22.88	25.31
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-33, 67	0, 67	-67, 33
LS Mean [2]		0.880		0.540
LS SE [2]		2.7468		3.3132
95% CI [2]		-4.580, 6.340		-6.044, 7.124
LS Mean Diff. to Placebo [2]		0.340		
LS SE Diff. to Placebo [2]		4.2015		
95% CI [2]		-8.016, 8.696		
One-sided p-value [2]		0.4678		
Hedge's G (95% CI)		0.02 [-0.531, 0.574]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	12.5	0.0	19.3	3.5
SD	20.30	25.40	32.04	29.18
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 100	-67, 67
LS Mean [2]		0.387		3.072
LS SE [2]		3.1926		3.8940
95% CI [2]		-5.958, 6.732		-4.667, 10.811
LS Mean Diff. to Placebo [2]		-2.685		
LS SE Diff. to Placebo [2]		4.9420		
95% CI [2]		-12.512, 7.142		
One-sided p-value [2]		0.7058		
Hedge's G (95% CI)		-0.15 [-0.720, 0.416]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	9.1	-3.0	15.0	3.5
SD	17.23	19.30	22.88	15.29
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-33, 33	0, 67	-33, 33
LS Mean [2]		-2.291		-0.601
LS SE [2]		2.3032		2.8237
95% CI [2]		-6.871, 2.289		-6.215, 5.013
LS Mean Diff. to Placebo [2]		-1.690		
LS SE Diff. to Placebo [2]		3.5200		
95% CI [2]		-8.696, 5.316		
One-sided p-value [2]		0.6838		
Hedge's G (95% CI)		-0.13 [-0.696, 0.434]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Dyspnoea				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	10.1	1.0	7.4	-2.0
SD	17.65	21.22	18.28	14.29
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-33, 67	0, 67	-33, 33
LS Mean [2]		-1.277		-2.783
LS SE [2]		2.4189		3.0987
95% CI [2]		-6.089, 3.535		-8.945, 3.380
LS Mean Diff. to Placebo [2]		1.505		
LS SE Diff. to Placebo [2]		3.7913		
95% CI [2]		-6.039, 9.050		
One-sided p-value [2]		0.3462		
Hedge's G (95% CI)		0.11 [-0.474, 0.697]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	11.1	0.0	8.3	2.1
SD	15.98	24.76	19.25	14.75
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 67	-33, 33
LS Mean [2]		0.084		-1.597
LS SE [2]		2.6843		3.4747
95% CI [2]		-5.269, 5.437		-8.529, 5.335
LS Mean Diff. to Placebo [2]		1.681		
LS SE Diff. to Placebo [2]		4.2729		
95% CI [2]		-6.850, 10.213		
One-sided p-value [2]		0.3476		
Hedge's G (95% CI)		0.11 [-0.493, 0.722]		

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	9.4	-1.0	9.5	4.8
SD	15.23	17.93	20.37	17.82
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 67	-33, 33
LS Mean [2]		-2.190		-1.218
LS SE [2]		2.3332		3.2646
95% CI [2]		-6.840, 2.459		-7.723, 5.288
LS Mean Diff. to Placebo [2]		-0.973		
LS SE Diff. to Placebo [2]		3.8706		
95% CI [2]		-8.694, 6.748		
One-sided p-value [2]		0.5989		
Hedge's G (95% CI)		-0.07 [-0.702, 0.554]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	9.7	0.0	8.8	1.8
SD	15.38	19.25	18.73	17.48
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 67	-33, 33
LS Mean [2]		-3.019		-1.221
LS SE [2]		2.4281		3.0268
95% CI [2]		-7.851, 1.814		-7.244, 4.802
LS Mean Diff. to Placebo [2]		-1.798		
LS SE Diff. to Placebo [2]		3.7336		
95% CI [2]		-9.234, 5.639		
One-sided p-value [2]		0.6842		
Hedge's G (95% CI)		-0.13 [-0.706, 0.437]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	12 (16.7)	12 (16.7)
Mean	9.2	-4.6	8.3	2.8
SD	15.16	19.36	20.72	17.16
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 67	-33, 33
LS Mean [2]		-2.846		-1.196
LS SE [2]		2.4476		3.5251
95% CI [2]		-7.737, 2.045		-8.244, 5.852
LS Mean Diff. to Placebo [2]		-1.650		
LS SE Diff. to Placebo [2]		4.2073		
95% CI [2]		-10.070, 6.770		
One-sided p-value [2]		0.6518		
Hedge's G (95% CI)		-0.13 [-0.799, 0.548]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	9.5	-3.2	3.0	0.0
SD	15.43	23.34	10.05	14.91
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 33	-33, 33
LS Mean [2]		-1.318		-5.659
LS SE [2]		2.8739		3.9785
95% CI [2]		-7.133, 4.498		-13.712, 2.395
LS Mean Diff. to Placebo [2]		4.341		
LS SE Diff. to Placebo [2]		4.8369		
95% CI [2]		-5.456, 14.138		
One-sided p-value [2]		0.1876		
Hedge's G (95% CI)		0.32 [-0.413, 1.055]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	10.5	0.0	6.7	0.0
SD	19.41	22.22	14.91	23.57
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-33, 67	0, 33	-33, 33
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	6.1	-3.0	5.6	5.6
SD	13.48	17.98	13.61	13.61
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 33	0, 33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 27				
n (%)	10 (14.3)	10 (14.3)	4 (5.6)	4 (5.6)
Mean	16.7	0.0	0.0	0.0
SD	17.57	22.22	0.00	0.00
Median	16.7	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 0	0, 0
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	5.6	-8.3	0.0	0.0
SD	12.97	20.72	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 0	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	2 (2.8)	2 (2.8)
Mean	9.1	-6.1	0.0	0.0
SD	15.57	25.03	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 0	0, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	12.5	-8.3	8.3	0.0
SD	17.25	23.57	16.67	27.22
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 33	-33, 33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	9.5	-9.5	0.0	0.0
SD	16.27	25.20	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 0	0, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	16.7	-5.6	0.0	0.0
SD	18.26	25.09	0.00	0.00
Median	16.7	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	6.7	-13.3		
SD	14.91	18.26		
Median	0.0	0.0		
Min, Max	0, 33	-33, 0		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Dyspnoea				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Dyspnoea				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	33.3	33.3		
SD	NA	NA		
Median	33.3	33.3		
Min, Max	33, 33	33, 33		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	9.5	-4.8	0.0	-33.3
SD	16.27	12.60	NA	NA
Median	0.0	0.0	0.0	-33.3
Min, Max	0, 33	-33, 0	0, 0	-33, -33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	47.1		49.0	
SD	37.85		37.52	
Median	33.3		33.3	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		-13.637		0.796
LS SE [2]		2.9572		3.1052
95% CI [2]		-19.487, -7.787		-5.340, 6.931
LS Mean Diff. to Placebo [2]		-14.433		
LS SE Diff. to Placebo [2]		3.9784		
95% CI [2]		-22.299, -6.566		
One-sided p-value [2]		0.9998		
Hedge's G (95% CI)		-0.58 [-0.924, -0.235]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 2				
n (%)	59 (84.3)	59 (84.3)	53 (73.6)	52 (72.2)
Mean	36.7	-10.7	45.9	-1.9
SD	33.16	31.83	32.83	28.33
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-100, 67
LS Mean [2]		-11.797		-2.255
LS SE [2]		3.7300		3.8563
95% CI [2]		-19.180, -4.415		-9.886, 5.376
LS Mean Diff. to Placebo [2]		-9.543		
LS SE Diff. to Placebo [2]		5.1214		
95% CI [2]		-19.685, 0.599		
One-sided p-value [2]		0.9675		
Hedge's G (95% CI)		-0.34 [-0.713, 0.038]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Insomnia				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	58 (80.6)	58 (80.6)
Mean	32.7	-13.8	46.6	-2.3
SD	34.28	30.27	36.91	30.50
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 33	0, 100	-100, 100
LS Mean [2]		-15.273		-3.289
LS SE [2]		3.8738		3.7900
95% CI [2]		-22.935, -7.611		-10.788, 4.210
LS Mean Diff. to Placebo [2]		-11.984		
LS SE Diff. to Placebo [2]		5.1748		
95% CI [2]		-22.228, -1.739		
One-sided p-value [2]		0.9889		
Hedge's G (95% CI)		-0.42 [-0.796, -0.043]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Insomnia				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	30.4	-7.2	48.6	-0.9
SD	30.49	30.56	35.65	31.36
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-100, 67
LS Mean [2]		-15.355		-1.489
LS SE [2]		4.3080		4.5425
95% CI [2]		-23.905, -6.804		-10.505, 7.527
LS Mean Diff. to Placebo [2]		-13.866		
LS SE Diff. to Placebo [2]		6.0765		
95% CI [2]		-25.937, -1.794		
One-sided p-value [2]		0.9876		
Hedge's G (95% CI)		-0.49 [-0.931, -0.046]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	40.3	-7.8	50.4	4.9
SD	36.77	36.97	35.06	28.44
Median	33.3	0.0	66.7	0.0
Min, Max	0, 100	-100, 67	0, 100	-33, 100
LS Mean [2]		-7.376		2.405
LS SE [2]		4.2577		4.3155
95% CI [2]		-15.812, 1.061		-6.147, 10.956
LS Mean Diff. to Placebo [2]		-9.780		
LS SE Diff. to Placebo [2]		5.8417		
95% CI [2]		-21.365, 1.804		
One-sided p-value [2]		0.9515		
Hedge's G (95% CI)		-0.35 [-0.783, 0.079]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	38.6	-2.6	46.3	4.8
SD	33.36	33.23	34.07	24.45
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-67, 67	0, 100	-67, 67
LS Mean [2]		-7.281		1.791
LS SE [2]		3.9354		4.0363
95% CI [2]		-15.088, 0.526		-6.213, 9.794
LS Mean Diff. to Placebo [2]		-9.072		
LS SE Diff. to Placebo [2]		5.3948		
95% CI [2]		-19.781, 1.637		
One-sided p-value [2]		0.9520		
Hedge's G (95% CI)		-0.38 [-0.840, 0.086]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	38.0	-10.1	50.5	-0.9
SD	34.57	39.53	35.68	25.80
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-67, 67
LS Mean [2]		-12.152		2.405
LS SE [2]		4.3510		4.5815
95% CI [2]		-20.779, -3.525		-6.678, 11.488
LS Mean Diff. to Placebo [2]		-14.557		
LS SE Diff. to Placebo [2]		6.1022		
95% CI [2]		-26.666, -2.448		
One-sided p-value [2]		0.9905		
Hedge's G (95% CI)		-0.52 [-0.969, -0.069]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	41.9	-3.9	54.4	5.7
SD	36.44	35.04	36.60	26.83
Median	33.3	0.0	66.7	0.0
Min, Max	0, 100	-100, 67	0, 100	-67, 67
LS Mean [2]		-8.939		5.346
LS SE [2]		4.1741		4.6573
95% CI [2]		-17.220, -0.657		-3.889, 14.582
LS Mean Diff. to Placebo [2]		-14.285		
LS SE Diff. to Placebo [2]		6.0496		
95% CI [2]		-26.292, -2.278		
One-sided p-value [2]		0.9899		
Hedge's G (95% CI)		-0.54 [-1.019, -0.060]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Insomnia				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	33.3	-11.4	49.5	8.8
SD	33.72	33.68	38.24	28.79
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 33	0, 100	-67, 100
LS Mean [2]		-12.996		5.410
LS SE [2]		3.9916		4.3039
95% CI [2]		-20.902, -5.090		-3.112, 13.931
LS Mean Diff. to Placebo [2]		-18.405		
LS SE Diff. to Placebo [2]		5.6318		
95% CI [2]		-29.567, -7.243		
One-sided p-value [2]		0.9993		
Hedge's G (95% CI)		-0.71 [-1.172, -0.250]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	36.8	-5.3	56.0	6.0
SD	34.48	36.78	35.20	28.77
Median	33.3	0.0	66.7	0.0
Min, Max	0, 100	-100, 67	0, 100	-33, 100
LS Mean [2]		-12.209		2.300
LS SE [2]		4.1779		4.5662
95% CI [2]		-20.494, -3.924		-6.752, 11.352
LS Mean Diff. to Placebo [2]		-14.509		
LS SE Diff. to Placebo [2]		5.9806		
95% CI [2]		-26.378, -2.640		
One-sided p-value [2]		0.9914		
Hedge's G (95% CI)		-0.58 [-1.076, -0.080]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Insomnia				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	35.3	-11.8	52.6	7.7
SD	31.72	38.39	34.22	19.57
Median	33.3	0.0	50.0	0.0
Min, Max	0, 100	-100, 67	0, 100	-33, 33
LS Mean [2]		-14.286		2.770
LS SE [2]		4.4115		4.8192
95% CI [2]		-23.054, -5.518		-6.801, 12.342
LS Mean Diff. to Placebo [2]		-17.056		
LS SE Diff. to Placebo [2]		6.3256		
95% CI [2]		-29.640, -4.473		
One-sided p-value [2]		0.9957		
Hedge's G (95% CI)		-0.68 [-1.201, -0.151]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	30.3	-16.2	45.8	2.8
SD	31.58	39.19	33.78	25.85
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-67, 33
LS Mean [2]		-17.797		-0.371
LS SE [2]		4.4455		4.9337
95% CI [2]		-26.633, -8.961		-10.170, 9.428
LS Mean Diff. to Placebo [2]		-17.426		
LS SE Diff. to Placebo [2]		6.4373		
95% CI [2]		-30.232, -4.621		
One-sided p-value [2]		0.9959		
Hedge's G (95% CI)		-0.70 [-1.239, -0.157]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	35.4	-15.2	49.3	3.0
SD	32.21	32.37	28.19	27.04
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 33	0, 100	-67, 67
LS Mean [2]		-17.599		3.890
LS SE [2]		3.7917		4.3400
95% CI [2]		-25.134, -10.063		-4.724, 12.503
LS Mean Diff. to Placebo [2]		-21.488		
LS SE Diff. to Placebo [2]		5.5290		
95% CI [2]		-32.481, -10.495		
One-sided p-value [2]		0.9999		
Hedge's G (95% CI)		-1.01 [-1.584, -0.441]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	34.3	-12.1	51.5	1.6
SD	34.85	39.81	36.70	30.69
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-67, 33
LS Mean [2]		-12.700		2.057
LS SE [2]		4.4184		5.1243
95% CI [2]		-21.470, -3.929		-8.110, 12.224
LS Mean Diff. to Placebo [2]		-14.757		
LS SE Diff. to Placebo [2]		6.5701		
95% CI [2]		-27.805, -1.708		
One-sided p-value [2]		0.9865		
Hedge's G (95% CI)		-0.60 [-1.157, -0.040]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	41.9	-9.7	49.3	1.5
SD	38.46	40.55	41.28	28.13
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-67, 33
LS Mean [2]		-9.325		0.702
LS SE [2]		4.6540		5.2423
95% CI [2]		-18.561, -0.089		-9.696, 11.101
LS Mean Diff. to Placebo [2]		-10.027		
LS SE Diff. to Placebo [2]		6.8109		
95% CI [2]		-23.553, 3.498		
One-sided p-value [2]		0.9278		
Hedge's G (95% CI)		-0.40 [-0.947, 0.156]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Insomnia				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	32.4	-11.8	50.0	-5.0
SD	32.29	33.72	33.33	32.94
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 33	0, 100	-67, 33
LS Mean [2]		-14.705		2.779
LS SE [2]		4.2266		5.0589
95% CI [2]		-23.104, -6.307		-7.269, 12.827
LS Mean Diff. to Placebo [2]		-17.484		
LS SE Diff. to Placebo [2]		6.4149		
95% CI [2]		-30.237, -4.731		
One-sided p-value [2]		0.9961		
Hedge's G (95% CI)		-0.73 [-1.300, -0.161]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	34.4	-13.5	47.4	0.0
SD	33.32	38.67	38.99	29.40
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-67, 33
LS Mean [2]		-14.737		3.326
LS SE [2]		4.4522		5.3303
95% CI [2]		-23.582, -5.892		-7.262, 13.915
LS Mean Diff. to Placebo [2]		-18.063		
LS SE Diff. to Placebo [2]		6.7551		
95% CI [2]		-31.491, -4.636		
One-sided p-value [2]		0.9955		
Hedge's G (95% CI)		-0.74 [-1.323, -0.152]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	34.3	-12.1	48.3	1.8
SD	35.83	38.92	29.57	20.71
Median	33.3	0.0	50.0	0.0
Min, Max	0, 100	-100, 67	0, 100	-33, 33
LS Mean [2]		-14.601		-2.629
LS SE [2]		4.1689		5.0459
95% CI [2]		-22.884, -6.318		-12.650, 7.392
LS Mean Diff. to Placebo [2]		-11.972		
LS SE Diff. to Placebo [2]		6.3464		
95% CI [2]		-24.590, 0.646		
One-sided p-value [2]		0.9687		
Hedge's G (95% CI)		-0.51 [-1.088, 0.058]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	36.4	-5.1	37.0	-2.0
SD	35.71	46.49	30.01	24.92
Median	33.3	0.0	33.3	0.0
Min, Max	0, 100	-100, 67	0, 100	-67, 33
LS Mean [2]		-7.093		-6.718
LS SE [2]		4.5993		5.8153
95% CI [2]		-16.229, 2.044		-18.265, 4.828
LS Mean Diff. to Placebo [2]		-0.375		
LS SE Diff. to Placebo [2]		7.2009		
95% CI [2]		-14.685, 13.935		
One-sided p-value [2]		0.5207		
Hedge's G (95% CI)		-0.01 [-0.600, 0.571]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	27.8	-20.0	54.2	0.0
SD	27.80	34.57	36.26	27.22
Median	33.3	0.0	66.7	0.0
Min, Max	0, 100	-100, 33	0, 100	-33, 33
LS Mean [2]		-21.332		3.185
LS SE [2]		3.9234		4.9496
95% CI [2]		-29.131, -13.533		-6.657, 13.027
LS Mean Diff. to Placebo [2]		-24.517		
LS SE Diff. to Placebo [2]		6.1137		
95% CI [2]		-36.684, -12.351		
One-sided p-value [2]		>0.9999		
Hedge's G (95% CI)		-1.15 [-1.802, -0.501]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	31.3	-16.7	47.6	-2.4
SD	32.72	32.79	38.60	35.72
Median	33.3	0.0	50.0	0.0
Min, Max	0, 100	-100, 33	0, 100	-67, 33
LS Mean [2]		-16.737		-2.384
LS SE [2]		4.1486		5.5869
95% CI [2]		-24.985, -8.490		-13.484, 8.716
LS Mean Diff. to Placebo [2]		-14.353		
LS SE Diff. to Placebo [2]		6.7721		
95% CI [2]		-27.824, -0.883		
One-sided p-value [2]		0.9815		
Hedge's G (95% CI)		-0.62 [-1.261, 0.020]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	31.2	-17.2	50.9	-3.5
SD	33.26	40.25	32.14	33.14
Median	33.3	0.0	66.7	0.0
Min, Max	0, 100	-100, 33	0, 100	-67, 67
LS Mean [2]		-17.983		0.367
LS SE [2]		4.5123		5.5461
95% CI [2]		-26.962, -9.005		-10.664, 11.398
LS Mean Diff. to Placebo [2]		-18.350		
LS SE Diff. to Placebo [2]		6.9658		
95% CI [2]		-32.218, -4.482		
One-sided p-value [2]		0.9949		
Hedge's G (95% CI)		-0.74 [-1.330, -0.152]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	36.8	-10.3	56.4	2.6
SD	34.90	34.62	34.39	31.80
Median	33.3	0.0	66.7	0.0
Min, Max	0, 100	-100, 33	0, 100	-67, 33
LS Mean [2]		-13.836		4.934
LS SE [2]		4.4472		6.0688
95% CI [2]		-22.697, -4.976		-7.161, 17.029
LS Mean Diff. to Placebo [2]		-18.770		
LS SE Diff. to Placebo [2]		7.3594		
95% CI [2]		-33.449, -4.091		
One-sided p-value [2]		0.9935		
Hedge's G (95% CI)		-0.79 [-1.464, -0.113]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 24				
n (%)	20 (28.6)	20 (28.6)	11 (15.3)	11 (15.3)
Mean	25.0	-15.0	33.3	-12.1
SD	30.35	31.48	25.82	26.97
Median	16.7	0.0	33.3	0.0
Min, Max	0, 100	-100, 33	0, 67	-67, 33
LS Mean [2]		-17.542		-6.233
LS SE [2]		4.0007		5.1397
95% CI [2]		-25.581, -9.504		-16.563, 4.096
LS Mean Diff. to Placebo [2]		-11.309		
LS SE Diff. to Placebo [2]		6.3399		
95% CI [2]		-24.067, 1.449		
One-sided p-value [2]		0.9595		
Hedge's G (95% CI)		-0.63 [-1.378, 0.126]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	17.5	-17.5	53.3	-20.0
SD	25.74	35.78	29.81	38.01
Median	0.0	0.0	33.3	-33.3
Min, Max	0, 100	-100, 33	33, 100	-67, 33
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	21.2	-21.2	66.7	-5.6
SD	30.81	42.88	36.51	25.09
Median	0.0	0.0	66.7	0.0
Min, Max	0, 100	-100, 33	0, 100	-33, 33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Insomnia				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	27.8	-5.6	83.3	8.3
SD	34.33	31.25	19.25	16.67
Median	16.7	0.0	83.3	0.0
Min, Max	0, 100	-67, 33	67, 100	0, 33
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	41.7	0.0	66.7	16.7
SD	37.94	34.82	47.14	23.57
Median	33.3	0.0	66.7	16.7
Min, Max	0, 100	-67, 67	33, 100	0, 33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	30.3	-6.1	66.7	0.0
SD	34.82	20.10	33.33	0.00
Median	33.3	0.0	66.7	0.0
Min, Max	0, 100	-33, 33	33, 100	0, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	20.8	-12.5	58.3	-16.7
SD	24.80	30.54	50.00	43.03
Median	16.7	0.0	66.7	-16.7
Min, Max	0, 67	-67, 33	0, 100	-67, 33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	28.6	-19.0	58.3	8.3
SD	12.60	37.80	41.94	31.91
Median	33.3	0.0	66.7	16.7
Min, Max	0, 33	-67, 33	0, 100	-33, 33
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	38.9	-11.1	50.0	0.0
SD	25.09	27.22	23.57	0.00
Median	33.3	-16.7	50.0	0.0
Min, Max	0, 67	-33, 33	33, 67	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	33.3	-13.3		
SD	23.57	38.01		
Median	33.3	0.0		
Min, Max	0, 67	-67, 33		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Insomnia				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	66.7	0.0		
SD	NA	NA		
Median	66.7	0.0		
Min, Max	67, 67	0, 0		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	52.4	-9.5	66.7	-33.3
SD	26.23	31.71	NA	NA
Median	33.3	0.0	66.7	-33.3
Min, Max	33, 100	-67, 33	67, 67	-33, -33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	14.8		17.6	
SD	25.15		27.05	
Median	0.0		0.0	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		0.858		-3.223
LS SE [2]		1.9867		2.0874
95% CI [2]		-3.070, 4.785		-7.345, 0.899
LS Mean Diff. to Placebo [2]		4.081		
LS SE Diff. to Placebo [2]		2.6898		
95% CI [2]		-1.236, 9.397		
One-sided p-value [2]		0.0657		
Hedge's G (95% CI)		0.24 [-0.095, 0.582]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	53 (73.6)	52 (72.2)
Mean	30.6	16.1	16.4	-3.2
SD	31.47	33.33	24.13	27.42
Median	33.3	0.0	0.0	0.0
Min, Max	0, 100	-33, 100	0, 100	-67, 67
LS Mean [2]		17.897		1.179
LS SE [2]		3.8221		4.0275
95% CI [2]		10.328, 25.465		-6.794, 9.152
LS Mean Diff. to Placebo [2]		16.717		
LS SE Diff. to Placebo [2]		5.4377		
95% CI [2]		5.946, 27.488		
One-sided p-value [2]		0.0013		
Hedge's G (95% CI)		0.57 [0.191, 0.948]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	18.2	4.4	11.9	-4.5
SD	27.40	24.49	19.34	22.71
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 67	0, 67	-67, 33
LS Mean [2]		5.122		-2.669
LS SE [2]		3.0951		3.0214
95% CI [2]		-1.006, 11.250		-8.654, 3.316
LS Mean Diff. to Placebo [2]		7.791		
LS SE Diff. to Placebo [2]		4.1929		
95% CI [2]		-0.518, 16.100		
One-sided p-value [2]		0.0329		
Hedge's G (95% CI)		0.34 [-0.033, 0.714]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 4				
n (%)	45 (64.3)	45 (64.3)	37 (51.4)	36 (50.0)
Mean	16.3	5.2	9.9	-11.1
SD	24.23	27.48	19.03	26.43
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 67	-100, 33
LS Mean [2]		4.783		-6.649
LS SE [2]		3.1485		3.3766
95% CI [2]		-1.462, 11.028		-13.345, 0.048
LS Mean Diff. to Placebo [2]		11.432		
LS SE Diff. to Placebo [2]		4.5080		
95% CI [2]		2.484, 20.379		
One-sided p-value [2]		0.0064		
Hedge's G (95% CI)		0.55 [0.105, 0.998]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	14.0	-0.8	9.8	-6.5
SD	25.44	26.71	17.07	26.05
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 67	-100, 33
LS Mean [2]		1.638		-4.069
LS SE [2]		2.9596		3.0122
95% CI [2]		-4.227, 7.503		-10.039, 1.900
LS Mean Diff. to Placebo [2]		5.707		
LS SE Diff. to Placebo [2]		4.0857		
95% CI [2]		-2.396, 13.810		
One-sided p-value [2]		0.0827		
Hedge's G (95% CI)		0.29 [-0.135, 0.725]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	13.2	1.8	11.1	-1.9
SD	26.33	27.89	17.82	22.78
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 67	-67, 33
LS Mean [2]		1.911		-3.202
LS SE [2]		3.2496		3.3404
95% CI [2]		-4.539, 8.361		-9.830, 3.425
LS Mean Diff. to Placebo [2]		5.113		
LS SE Diff. to Placebo [2]		4.5393		
95% CI [2]		-3.901, 14.127		
One-sided p-value [2]		0.1314		
Hedge's G (95% CI)		0.26 [-0.204, 0.718]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	17.8	3.9	9.9	-9.3
SD	32.00	31.04	22.03	23.38
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 100	-67, 33
LS Mean [2]		4.183		-5.707
LS SE [2]		3.5672		3.7928
95% CI [2]		-2.890, 11.255		-13.225, 1.811
LS Mean Diff. to Placebo [2]		9.890		
LS SE Diff. to Placebo [2]		5.0905		
95% CI [2]		-0.208, 19.987		
One-sided p-value [2]		0.0274		
Hedge's G (95% CI)		0.43 [-0.020, 0.876]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	13.2	-1.6	15.6	0.0
SD	23.16	24.07	27.31	21.82
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 67	0, 100	-33, 67
LS Mean [2]		-1.867		-2.611
LS SE [2]		2.8069		3.1545
95% CI [2]		-7.433, 3.698		-8.864, 3.642
LS Mean Diff. to Placebo [2]		0.744		
LS SE Diff. to Placebo [2]		4.0941		
95% CI [2]		-7.378, 8.866		
One-sided p-value [2]		0.4281		
Hedge's G (95% CI)		0.04 [-0.429, 0.513]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	12.1	-3.0	13.3	-2.9
SD	22.84	23.64	27.06	27.67
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 100	-100, 67
LS Mean [2]		-0.926		-2.942
LS SE [2]		2.9605		3.2150
95% CI [2]		-6.791, 4.938		-9.309, 3.425
LS Mean Diff. to Placebo [2]		2.015		
LS SE Diff. to Placebo [2]		4.2312		
95% CI [2]		-6.372, 10.403		
One-sided p-value [2]		0.3174		
Hedge's G (95% CI)		0.10 [-0.343, 0.553]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	7.9	-4.4	17.9	4.8
SD	18.07	24.72	27.94	28.28
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 100	-67, 67
LS Mean [2]		-2.843		1.042
LS SE [2]		3.0370		3.3587
95% CI [2]		-8.869, 3.183		-5.621, 7.704
LS Mean Diff. to Placebo [2]		-3.885		
LS SE Diff. to Placebo [2]		4.4037		
95% CI [2]		-12.629, 4.860		
One-sided p-value [2]		0.8100		
Hedge's G (95% CI)		-0.21 [-0.701, 0.278]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	15.7	1.0	6.4	1.3
SD	24.94	26.57	21.12	17.59
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 100	-67, 33
LS Mean [2]		1.860		-5.474
LS SE [2]		2.8843		3.2260
95% CI [2]		-3.862, 7.581		-11.871, 0.923
LS Mean Diff. to Placebo [2]		7.334		
LS SE Diff. to Placebo [2]		4.2124		
95% CI [2]		-1.029, 15.697		
One-sided p-value [2]		0.0425		
Hedge's G (95% CI)		0.44 [-0.076, 0.957]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	24 (33.3)	24 (33.3)
Mean	19.2	6.1	4.2	0.0
SD	30.08	24.23	11.26	19.66
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 67	0, 33	-67, 33
LS Mean [2]		4.260		-2.711
LS SE [2]		2.9778		3.4153
95% CI [2]		-1.651, 10.170		-9.488, 4.065
LS Mean Diff. to Placebo [2]		6.971		
LS SE Diff. to Placebo [2]		4.4070		
95% CI [2]		-1.783, 15.725		
One-sided p-value [2]		0.0586		
Hedge's G (95% CI)		0.41 [-0.120, 0.942]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	19.2	0.0	5.8	0.0
SD	30.08	25.00	12.92	10.29
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 67	0, 33	-33, 33
LS Mean [2]		2.003		-5.524
LS SE [2]		2.7219		3.1796
95% CI [2]		-3.404, 7.410		-11.835, 0.788
LS Mean Diff. to Placebo [2]		7.527		
LS SE Diff. to Placebo [2]		4.1055		
95% CI [2]		-0.634, 15.688		
One-sided p-value [2]		0.0351		
Hedge's G (95% CI)		0.49 [-0.057, 1.037]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	11.1	0.0	7.6	-4.8
SD	21.52	22.05	14.30	24.23
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 33	0, 33	-67, 33
LS Mean [2]		0.731		-7.372
LS SE [2]		2.8640		3.3581
95% CI [2]		-4.969, 6.431		-14.054, -0.690
LS Mean Diff. to Placebo [2]		8.103		
LS SE Diff. to Placebo [2]		4.2860		
95% CI [2]		-0.435, 16.641		
One-sided p-value [2]		0.0313		
Hedge's G (95% CI)		0.50 [-0.051, 1.060]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	12.9	-2.2	14.5	1.5
SD	25.35	20.97	24.26	24.07
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 33	0, 67	-67, 67
LS Mean [2]		0.266		0.347
LS SE [2]		3.2603		3.7122
95% CI [2]		-6.222, 6.755		-7.039, 7.734
LS Mean Diff. to Placebo [2]		-0.081		
LS SE Diff. to Placebo [2]		4.8332		
95% CI [2]		-9.709, 9.547		
One-sided p-value [2]		0.5067		
Hedge's G (95% CI)		-0.00 [-0.551, 0.542]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	10.8	0.0	15.0	3.3
SD	21.27	21.71	20.16	28.41
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 67	-67, 67
LS Mean [2]		-0.412		2.799
LS SE [2]		2.9304		3.5352
95% CI [2]		-6.238, 5.415		-4.227, 9.826
LS Mean Diff. to Placebo [2]		-3.211		
LS SE Diff. to Placebo [2]		4.4739		
95% CI [2]		-12.112, 5.690		
One-sided p-value [2]		0.7625		
Hedge's G (95% CI)		-0.19 [-0.747, 0.360]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Appetite Loss				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	12.5	-2.1	8.8	3.5
SD	25.04	29.25	15.08	21.93
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 33	-33, 33
LS Mean [2]		-2.165		-2.797
LS SE [2]		3.1596		3.8986
95% CI [2]		-8.449, 4.120		-10.554, 4.960
LS Mean Diff. to Placebo [2]		0.632		
LS SE Diff. to Placebo [2]		4.9254		
95% CI [2]		-9.172, 10.437		
One-sided p-value [2]		0.4491		
Hedge's G (95% CI)		0.04 [-0.532, 0.604]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Appetite Loss				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	8.1	-6.1	10.0	1.8
SD	14.51	21.17	21.90	26.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 67	-67, 67
LS Mean [2]		-5.024		-4.603
LS SE [2]		2.2853		2.8299
95% CI [2]		-9.567, -0.482		-10.228, 1.022
LS Mean Diff. to Placebo [2]		-0.421		
LS SE Diff. to Placebo [2]		3.5066		
95% CI [2]		-7.398, 6.556		
One-sided p-value [2]		0.5476		
Hedge's G (95% CI)		-0.03 [-0.597, 0.532]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	14.1	3.0	14.8	2.0
SD	25.04	29.30	28.52	27.56
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 100	-67, 67
LS Mean [2]		1.888		-3.781
LS SE [2]		3.5764		4.6365
95% CI [2]		-5.237, 9.013		-13.016, 5.453
LS Mean Diff. to Placebo [2]		5.669		
LS SE Diff. to Placebo [2]		5.7356		
95% CI [2]		-5.763, 17.101		
One-sided p-value [2]		0.1631		
Hedge's G (95% CI)		0.28 [-0.305, 0.870]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	11.1	-2.2	8.3	6.3
SD	20.22	23.05	25.82	27.81
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 33	0, 100	-33, 100
LS Mean [2]		-0.523		-1.678
LS SE [2]		3.1616		4.1973
95% CI [2]		-6.815, 5.768		-10.033, 6.677
LS Mean Diff. to Placebo [2]		1.154		
LS SE Diff. to Placebo [2]		5.1559		
95% CI [2]		-9.115, 11.424		
One-sided p-value [2]		0.4117		
Hedge's G (95% CI)		0.07 [-0.541, 0.673]		

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	7.3	-5.2	7.1	2.4
SD	14.00	20.93	19.30	27.62
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 67	-67, 67
LS Mean [2]		-6.260		-4.662
LS SE [2]		2.2044		3.0563
95% CI [2]		-10.642, -1.878		-10.737, 1.413
LS Mean Diff. to Placebo [2]		-1.598		
LS SE Diff. to Placebo [2]		3.6327		
95% CI [2]		-8.827, 5.630		
One-sided p-value [2]		0.6694		
Hedge's G (95% CI)		-0.13 [-0.758, 0.500]		

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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	10.8	-4.3	5.3	-1.8
SD	19.98	22.35	12.49	23.50
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 33	0, 33	-67, 33
LS Mean [2]		-1.489		-5.150
LS SE [2]		2.7001		3.3539
95% CI [2]		-6.868, 3.891		-11.832, 1.532
LS Mean Diff. to Placebo [2]		3.661		
LS SE Diff. to Placebo [2]		4.2150		
95% CI [2]		-4.746, 12.068		
One-sided p-value [2]		0.1940		
Hedge's G (95% CI)		0.25 [-0.327, 0.819]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Appetite Loss				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	11.5	-4.6	5.1	-2.6
SD	24.03	19.36	12.52	25.32
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 33	0, 33	-67, 33
LS Mean [2]		-4.688		-4.547
LS SE [2]		2.2689		3.0701
95% CI [2]		-9.199, -0.176		-10.657, 1.564
LS Mean Diff. to Placebo [2]		-0.141		
LS SE Diff. to Placebo [2]		3.7181		
95% CI [2]		-7.546, 7.264		
One-sided p-value [2]		0.5151		
Hedge's G (95% CI)		-0.01 [-0.666, 0.643]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	9.5	1.6	6.1	-3.0
SD	21.46	26.82	20.10	31.46
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 67	-67, 67
LS Mean [2]		-0.618		-3.353
LS SE [2]		3.4483		4.4838
95% CI [2]		-7.549, 6.312		-12.371, 5.665
LS Mean Diff. to Placebo [2]		2.735		
LS SE Diff. to Placebo [2]		5.5345		
95% CI [2]		-8.402, 13.871		
One-sided p-value [2]		0.3118		
Hedge's G (95% CI)		0.17 [-0.559, 0.903]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	1.8	-7.0	20.0	13.3
SD	7.65	21.02	29.81	29.81
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 67	0, 67
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	6.1	-6.1	0.0	0.0
SD	13.48	25.03	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	8.3	0.0	8.3	8.3
SD	20.72	31.78	16.67	16.67
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-67, 67	0, 33	0, 33
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	8.3	-5.6	0.0	0.0
SD	15.08	23.92	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	6.1	-6.1	0.0	0.0
SD	13.48	29.13	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-67, 33	0, 0	0, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	8.3	-8.3	0.0	0.0
SD	15.43	23.57	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-33, 33	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	4.8	-19.0	0.0	0.0
SD	12.60	32.53	0.00	0.00
Median	0.0	-33.3	0.0	0.0
Min, Max	0, 33	-67, 33	0, 0	0, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	5.6	-16.7	0.0	0.0
SD	13.61	34.96	0.00	0.00
Median	0.0	-16.7	0.0	0.0
Min, Max	0, 33	-67, 33	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	6.7	-13.3		
SD	14.91	18.26		
Median	0.0	0.0		
Min, Max	0, 33	-33, 0		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Appetite Loss				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	66.7	33.3		
SD	NA	NA		
Median	66.7	33.3		
Min, Max	67, 67	33, 33		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	9.5	-9.5	0.0	-33.3
SD	25.20	16.27	NA	NA
Median	0.0	0.0	0.0	-33.3
Min, Max	0, 67	-33, 0	0, 0	-33, -33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	11.9		11.9	
SD	21.26		18.85	
Median	0.0		0.0	
Min, Max	0, 100		0, 67	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		-7.215		-0.554
LS SE [2]		1.5635		1.6449
95% CI [2]		-10.308, -4.122		-3.805, 2.696
LS Mean Diff. to Placebo [2]		-6.661		
LS SE Diff. to Placebo [2]		2.1638		
95% CI [2]		-10.941, -2.380		
One-sided p-value [2]		0.9987		
Hedge's G (95% CI)		-0.51 [-0.848, -0.163]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	52 (72.2)	51 (70.8)
Mean	7.8	-5.0	17.9	4.6
SD	18.78	21.98	24.22	24.06
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-67, 67	0, 100	-67, 67
LS Mean [2]		-4.340		3.395
LS SE [2]		2.5959		2.7438
95% CI [2]		-9.485, 0.804		-2.041, 8.831
LS Mean Diff. to Placebo [2]		-7.736		
LS SE Diff. to Placebo [2]		3.7164		
95% CI [2]		-15.103, -0.368		
One-sided p-value [2]		0.9801		
Hedge's G (95% CI)		-0.39 [-0.766, -0.012]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	12.6	0.6	13.0	1.1
SD	26.33	30.31	23.99	20.50
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-100, 100	0, 100	-67, 67
LS Mean [2]		0.256		1.602
LS SE [2]		3.2503		3.1650
95% CI [2]		-6.180, 6.692		-4.667, 7.871
LS Mean Diff. to Placebo [2]		-1.346		
LS SE Diff. to Placebo [2]		4.4832		
95% CI [2]		-10.226, 7.535		
One-sided p-value [2]		0.6177		
Hedge's G (95% CI)		-0.06 [-0.427, 0.315]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	5.8	-5.1	15.3	0.9
SD	14.58	22.19	24.34	18.66
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 33	0, 100	-33, 33
LS Mean [2]		-5.900		0.383
LS SE [2]		2.4184		2.6056
95% CI [2]		-10.696, -1.104		-4.783, 5.550
LS Mean Diff. to Placebo [2]		-6.283		
LS SE Diff. to Placebo [2]		3.4913		
95% CI [2]		-13.210, 0.644		
One-sided p-value [2]		0.9625		
Hedge's G (95% CI)		-0.39 [-0.831, 0.049]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	41 (56.9)	41 (56.9)
Mean	3.1	-9.3	13.8	1.6
SD	9.80	22.21	23.54	22.30
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 33	0, 67	-67, 67
LS Mean [2]		-7.541		0.280
LS SE [2]		2.6127		2.6730
95% CI [2]		-12.729, -2.353		-5.028, 5.588
LS Mean Diff. to Placebo [2]		-7.822		
LS SE Diff. to Placebo [2]		3.6737		
95% CI [2]		-15.120, -0.523		
One-sided p-value [2]		0.9820		
Hedge's G (95% CI)		-0.46 [-0.890, -0.023]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	4.4	-7.9	13.0	0.0
SD	17.62	26.21	19.96	18.08
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-100, 67	0, 67	-67, 33
LS Mean [2]		-5.398		-3.787
LS SE [2]		2.8094		2.9067
95% CI [2]		-10.985, 0.189		-9.566, 1.992
LS Mean Diff. to Placebo [2]		-1.611		
LS SE Diff. to Placebo [2]		3.9839		
95% CI [2]		-9.536, 6.314		
One-sided p-value [2]		0.6565		
Hedge's G (95% CI)		-0.09 [-0.553, 0.366]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	7.0	-6.2	14.4	1.9
SD	13.72	22.13	22.96	22.46
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 33	0, 67	-67, 67
LS Mean [2]		-5.473		-0.102
LS SE [2]		2.4665		2.6051
95% CI [2]		-10.364, -0.582		-5.267, 5.064
LS Mean Diff. to Placebo [2]		-5.371		
LS SE Diff. to Placebo [2]		3.5245		
95% CI [2]		-12.363, 1.621		
One-sided p-value [2]		0.9347		
Hedge's G (95% CI)		-0.34 [-0.783, 0.109]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 8				
n (%)	42 (60.0)	42 (60.0)	30 (41.7)	29 (40.3)
Mean	7.1	-5.6	16.7	2.3
SD	17.32	26.46	24.37	19.78
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 67	-67, 33
LS Mean [2]		-4.428		-1.271
LS SE [2]		2.7256		3.0922
95% CI [2]		-9.842, 0.986		-7.411, 4.869
LS Mean Diff. to Placebo [2]		-3.157		
LS SE Diff. to Placebo [2]		4.0660		
95% CI [2]		-11.235, 4.920		
One-sided p-value [2]		0.7803		
Hedge's G (95% CI)		-0.18 [-0.657, 0.291]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	34 (47.2)	33 (45.8)
Mean	2.3	-8.3	13.7	2.0
SD	11.13	25.03	23.38	21.95
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 100	-33, 67
LS Mean [2]		-8.021		-3.454
LS SE [2]		2.7268		3.0179
95% CI [2]		-13.440, -2.603		-9.449, 2.541
LS Mean Diff. to Placebo [2]		-4.567		
LS SE Diff. to Placebo [2]		4.0050		
95% CI [2]		-12.528, 3.394		
One-sided p-value [2]		0.8714		
Hedge's G (95% CI)		-0.26 [-0.710, 0.196]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	1.8	-7.9	20.2	7.1
SD	7.54	22.51	31.87	27.75
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 33	0, 100	-33, 100
LS Mean [2]		-9.049		3.649
LS SE [2]		2.9662		3.3126
95% CI [2]		-14.943, -3.156		-2.930, 10.229
LS Mean Diff. to Placebo [2]		-12.698		
LS SE Diff. to Placebo [2]		4.3975		
95% CI [2]		-21.437, -3.960		
One-sided p-value [2]		0.9976		
Hedge's G (95% CI)		-0.71 [-1.209, -0.204]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	2.0	-8.8	9.0	-3.8
SD	7.96	22.19	15.08	14.38
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 0	0, 33	-33, 33
LS Mean [2]		-8.914		-6.225
LS SE [2]		1.6266		1.8071
95% CI [2]		-12.146, -5.682		-9.814, -2.636
LS Mean Diff. to Placebo [2]		-2.689		
LS SE Diff. to Placebo [2]		2.3208		
95% CI [2]		-7.305, 1.927		
One-sided p-value [2]		0.8750		
Hedge's G (95% CI)		-0.29 [-0.800, 0.226]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 12				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	23 (31.9)
Mean	1.0	-12.1	11.6	-2.9
SD	5.80	23.30	16.23	13.90
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 0	0, 33	-33, 33
LS Mean [2]		-10.583		-3.563
LS SE [2]		1.6894		1.9427
95% CI [2]		-13.949, -7.218		-7.431, 0.305
LS Mean Diff. to Placebo [2]		-7.020		
LS SE Diff. to Placebo [2]		2.4738		
95% CI [2]		-11.954, -2.087		
One-sided p-value [2]		0.9970		
Hedge's G (95% CI)		-0.74 [-1.285, -0.186]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	4.0	-8.1	17.4	3.0
SD	18.18	26.39	24.35	20.34
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-100, 67	0, 67	-33, 67
LS Mean [2]		-7.730		-1.671
LS SE [2]		2.6337		3.0698
95% CI [2]		-12.971, -2.488		-7.778, 4.436
LS Mean Diff. to Placebo [2]		-6.058		
LS SE Diff. to Placebo [2]		3.9782		
95% CI [2]		-13.979, 1.863		
One-sided p-value [2]		0.9341		
Hedge's G (95% CI)		-0.41 [-0.953, 0.137]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 14				
n (%)	32 (45.7)	32 (45.7)	22 (30.6)	21 (29.2)
Mean	1.0	-8.3	16.7	1.6
SD	5.89	23.95	26.73	28.82
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 33	0, 100	-33, 100
LS Mean [2]		-8.939		-1.311
LS SE [2]		2.6529		3.1196
95% CI [2]		-14.223, -3.656		-7.522, 4.901
LS Mean Diff. to Placebo [2]		-7.628		
LS SE Diff. to Placebo [2]		4.0460		
95% CI [2]		-15.689, 0.433		
One-sided p-value [2]		0.9684		
Hedge's G (95% CI)		-0.52 [-1.077, 0.041]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	4.3	-8.6	15.9	3.0
SD	11.36	25.77	26.34	28.93
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 33	0, 100	-67, 100
LS Mean [2]		-5.659		-0.664
LS SE [2]		3.0078		3.4546
95% CI [2]		-11.652, 0.333		-7.545, 6.217
LS Mean Diff. to Placebo [2]		-4.995		
LS SE Diff. to Placebo [2]		4.5268		
95% CI [2]		-14.017, 4.027		
One-sided p-value [2]		0.8633		
Hedge's G (95% CI)		-0.30 [-0.852, 0.247]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 16				
n (%)	33 (47.1)	33 (47.1)	19 (26.4)	19 (26.4)
Mean	0.0	-12.1	21.1	8.8
SD	0.00	23.30	25.36	21.78
Median	0.0	0.0	0.0	0.0
Min, Max	0, 0	-100, 0	0, 67	-33, 33
LS Mean [2]		-10.228		3.144
LS SE [2]		2.3761		2.9339
95% CI [2]		-14.969, -5.486		-2.710, 8.997
LS Mean Diff. to Placebo [2]		-13.371		
LS SE Diff. to Placebo [2]		3.7125		
95% CI [2]		-20.783, -5.960		
One-sided p-value [2]		0.9997		
Hedge's G (95% CI)		-1.00 [-1.598, -0.406]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 17				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	2.2	-9.7	10.5	0.0
SD	8.32	24.64	22.37	15.71
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 33	0, 67	-33, 33
LS Mean [2]		-8.763		-3.809
LS SE [2]		2.3031		2.7912
95% CI [2]		-13.362, -4.163		-9.384, 1.765
LS Mean Diff. to Placebo [2]		-4.953		
LS SE Diff. to Placebo [2]		3.5557		
95% CI [2]		-12.059, 2.152		
One-sided p-value [2]		0.9157		
Hedge's G (95% CI)		-0.39 [-0.970, 0.183]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	2.0	-9.1	20.0	7.0
SD	8.08	23.97	27.36	17.84
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 33	0, 67	-33, 33
LS Mean [2]		-9.234		2.711
LS SE [2]		2.2895		2.8370
95% CI [2]		-13.789, -4.679		-2.931, 8.353
LS Mean Diff. to Placebo [2]		-11.945		
LS SE Diff. to Placebo [2]		3.5798		
95% CI [2]		-19.070, -4.821		
One-sided p-value [2]		0.9994		
Hedge's G (95% CI)		-0.93 [-1.520, -0.336]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 19				
n (%)	33 (47.1)	33 (47.1)	18 (25.0)	17 (23.6)
Mean	2.0	-8.1	18.5	7.8
SD	8.08	23.61	28.52	18.74
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 33	0, 100	0, 67
LS Mean [2]		-7.947		3.629
LS SE [2]		2.7842		3.6126
95% CI [2]		-13.505, -2.389		-3.581, 10.839
LS Mean Diff. to Placebo [2]		-11.576		
LS SE Diff. to Placebo [2]		4.4981		
95% CI [2]		-20.558, -2.594		
One-sided p-value [2]		0.9938		
Hedge's G (95% CI)		-0.74 [-1.343, -0.137]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	5.6	-6.7	12.5	2.1
SD	15.37	28.23	20.64	8.33
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 67	0, 33
LS Mean [2]		-3.296		3.003
LS SE [2]		3.0432		3.9867
95% CI [2]		-9.399, 2.807		-4.990, 10.996
LS Mean Diff. to Placebo [2]		-6.299		
LS SE Diff. to Placebo [2]		4.9656		
95% CI [2]		-16.261, 3.664		
One-sided p-value [2]		0.8949		
Hedge's G (95% CI)		-0.38 [-0.989, 0.235]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	1.0	-9.4	9.5	-2.4
SD	5.89	22.77	20.37	20.52
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 0	0, 67	-67, 33
LS Mean [2]		-10.035		-3.704
LS SE [2]		1.7332		2.3591
95% CI [2]		-13.487, -6.584		-8.404, 0.997
LS Mean Diff. to Placebo [2]		-6.332		
LS SE Diff. to Placebo [2]		2.8493		
95% CI [2]		-12.013, -0.650		
One-sided p-value [2]		0.9853		
Hedge's G (95% CI)		-0.65 [-1.295, -0.011]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	1.1	-10.8	15.8	1.8
SD	5.99	23.39	25.74	17.48
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	-100, 0	0, 67	-33, 33
LS Mean [2]		-10.452		0.019
LS SE [2]		2.0247		2.4512
95% CI [2]		-14.478, -6.425		-4.858, 4.896
LS Mean Diff. to Placebo [2]		-10.471		
LS SE Diff. to Placebo [2]		3.1120		
95% CI [2]		-16.666, -4.276		
One-sided p-value [2]		0.9994		
Hedge's G (95% CI)		-0.95 [-1.548, -0.347]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Constipation				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	8.0	-4.6	12.8	2.6
SD	21.19	29.17	25.60	9.25
Median	0.0	0.0	0.0	0.0
Min, Max	0, 100	-100, 67	0, 67	0, 33
LS Mean [2]		-4.057		0.506
LS SE [2]		2.9108		3.9466
95% CI [2]		-9.860, 1.747		-7.374, 8.385
LS Mean Diff. to Placebo [2]		-4.563		
LS SE Diff. to Placebo [2]		4.8598		
95% CI [2]		-14.263, 5.138		
One-sided p-value [2]		0.8244		
Hedge's G (95% CI)		-0.29 [-0.951, 0.364]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Constipation				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	0.0	-7.9	6.1	-3.0
SD	0.00	23.34	13.48	10.05
Median	0.0	0.0	0.0	0.0
Min, Max	0, 0	-100, 0	0, 33	-33, 0
LS Mean [2]		-10.210		-5.503
LS SE [2]		1.3915		1.8368
95% CI [2]		-13.017, -7.403		-9.207, -1.800
LS Mean Diff. to Placebo [2]		-4.707		
LS SE Diff. to Placebo [2]		2.2287		
95% CI [2]		-9.201, -0.212		
One-sided p-value [2]		0.9797		
Hedge's G (95% CI)		-0.73 [-1.481, 0.021]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	0.0	-8.8	13.3	-6.7
SD	0.00	24.45	18.26	14.91
Median	0.0	0.0	0.0	0.0
Min, Max	0, 0	-100, 0	0, 33	-33, 0
Cycle 26				
n (%)	10 (14.3)	10 (14.3)	6 (8.3)	6 (8.3)
Mean	0.0	-13.3	16.7	-5.6
SD	0.00	32.20	18.26	13.61
Median	0.0	0.0	16.7	0.0
Min, Max	0, 0	-100, 0	0, 33	-33, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	5.6	-5.6	8.3	-8.3
SD	19.25	37.15	16.67	16.67
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	-100, 67	0, 33	-33, 0
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	0.0	-13.9	0.0	0.0
SD	0.00	30.01	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 0	-100, 0	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	2 (2.8)	2 (2.8)
Mean	0.0	-15.2	16.7	0.0
SD	0.00	31.14	23.57	0.00
Median	0.0	0.0	16.7	0.0
Min, Max	0, 0	-100, 0	0, 33	0, 0
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	0.0	-12.5	8.3	0.0
SD	0.00	35.36	16.67	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 0	-100, 0	0, 33	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	0.0	-23.8	0.0	0.0
SD	0.00	37.09	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 0	-100, 0	0, 0	0, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	0.0	-27.8	0.0	0.0
SD	0.00	38.97	0.00	0.00
Median	0.0	-16.7	0.0	0.0
Min, Max	0, 0	-100, 0	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	6.7	-26.7		
SD	14.91	43.46		
Median	0.0	0.0		
Min, Max	0, 33	-100, 0		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Constipation				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	4.8	0.0	0.0	0.0
SD	12.60	0.00	NA	NA
Median	0.0	0.0	0.0	0.0
Min, Max	0, 33	0, 0	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Baseline [1]				
n (%)	69 (98.6)		70 (97.2)	
Mean	11.6		8.1	
SD	24.14		18.33	
Median	0.0		0.0	
Min, Max	0, 100		0, 100	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Effect over Study Duration				
n (%)		67 (95.7)		67 (93.1)
LS Mean [2]		33.006		3.333
LS SE [2]		3.3013		3.3462
95% CI [2]		26.480, 39.532		-3.275, 9.942
LS Mean Diff. to Placebo [2]		29.673		
LS SE Diff. to Placebo [2]		4.3093		
95% CI [2]		21.157, 38.188		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.09 [0.728, 1.454]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 2				
n (%)	60 (85.7)	59 (84.3)	53 (73.6)	52 (72.2)
Mean	52.2	41.2	17.0	6.4
SD	35.98	39.80	26.65	24.73
Median	66.7	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 100	-33, 100
LS Mean [2]		43.012		6.713
LS SE [2]		4.5040		4.5748
95% CI [2]		34.099, 51.925		-2.340, 15.766
LS Mean Diff. to Placebo [2]		36.299		
LS SE Diff. to Placebo [2]		6.1363		
95% CI [2]		24.145, 48.452		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.07 [0.674, 1.471]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 3				
n (%)	53 (75.7)	52 (74.3)	59 (81.9)	59 (81.9)
Mean	52.8	42.3	9.6	0.6
SD	36.65	44.83	19.62	21.88
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 100	-67, 67
LS Mean [2]		44.104		0.182
LS SE [2]		4.1879		3.9995
95% CI [2]		35.826, 52.382		-7.729, 8.093
LS Mean Diff. to Placebo [2]		43.922		
LS SE Diff. to Placebo [2]		5.4746		
95% CI [2]		33.089, 54.754		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.44 [1.023, 1.859]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 4				
n (%)	46 (65.7)	45 (64.3)	37 (51.4)	36 (50.0)
Mean	55.8	48.1	9.9	0.9
SD	37.22	41.17	19.03	16.88
Median	66.7	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 67	-33, 33
LS Mean [2]		46.171		0.671
LS SE [2]		4.4387		4.5735
95% CI [2]		37.384, 54.958		-8.383, 9.726
LS Mean Diff. to Placebo [2]		45.500		
LS SE Diff. to Placebo [2]		6.0755		
95% CI [2]		33.462, 57.538		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.58 [1.080, 2.083]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 5				
n (%)	43 (61.4)	42 (60.0)	41 (56.9)	41 (56.9)
Mean	48.8	38.1	8.9	0.8
SD	35.15	40.71	19.75	15.79
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 100	-33, 33
LS Mean [2]		37.530		-0.642
LS SE [2]		4.1189		4.0634
95% CI [2]		29.379, 45.680		-8.686, 7.401
LS Mean Diff. to Placebo [2]		38.172		
LS SE Diff. to Placebo [2]		5.4734		
95% CI [2]		27.330, 49.014		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.45 [0.965, 1.931]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 6				
n (%)	38 (54.3)	37 (52.9)	36 (50.0)	35 (48.6)
Mean	48.2	39.6	10.2	2.9
SD	35.26	40.70	20.81	23.39
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 67	-67, 67
LS Mean [2]		34.455		-0.325
LS SE [2]		4.6733		4.6957
95% CI [2]		25.184, 43.727		-9.640, 8.990
LS Mean Diff. to Placebo [2]		34.780		
LS SE Diff. to Placebo [2]		6.3233		
95% CI [2]		22.224, 47.337		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.24 [0.733, 1.742]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 7				
n (%)	43 (61.4)	42 (60.0)	37 (51.4)	36 (50.0)
Mean	41.1	31.0	15.3	5.6
SD	37.68	38.53	27.88	23.23
Median	33.3	16.7	0.0	0.0
Min, Max	0, 100	-33, 100	0, 100	-33, 100
LS Mean [2]		30.437		6.072
LS SE [2]		4.3866		4.4836
95% CI [2]		21.758, 39.115		-2.800, 14.943
LS Mean Diff. to Placebo [2]		24.365		
LS SE Diff. to Placebo [2]		5.9766		
95% CI [2]		12.530, 36.201		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.88 [0.412, 1.345]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 8				
n (%)	43 (61.4)	42 (60.0)	30 (41.7)	29 (40.3)
Mean	46.5	34.9	14.4	2.3
SD	35.74	41.62	25.80	19.78
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 100	-33, 67
LS Mean [2]		33.668		1.975
LS SE [2]		4.0245		4.2991
95% CI [2]		25.707, 41.628		-6.527, 10.476
LS Mean Diff. to Placebo [2]		31.693		
LS SE Diff. to Placebo [2]		5.5803		
95% CI [2]		20.649, 42.737		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.27 [0.754, 1.788]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 9				
n (%)	44 (62.9)	43 (61.4)	35 (48.6)	34 (47.2)
Mean	46.2	34.9	9.5	2.0
SD	34.64	39.81	19.08	16.29
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 67	-33, 67
LS Mean [2]		34.109		3.398
LS SE [2]		3.8966		4.0539
95% CI [2]		26.402, 41.816		-4.619, 11.415
LS Mean Diff. to Placebo [2]		30.710		
LS SE Diff. to Placebo [2]		5.2991		
95% CI [2]		20.221, 41.200		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.24 [0.751, 1.733]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 10				
n (%)	38 (54.3)	37 (52.9)	28 (38.9)	28 (38.9)
Mean	43.0	33.3	15.5	8.3
SD	32.80	36.85	24.82	28.15
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 100	-33, 100
LS Mean [2]		33.524		8.267
LS SE [2]		4.3541		4.6339
95% CI [2]		24.901, 42.147		-0.910, 17.443
LS Mean Diff. to Placebo [2]		25.257		
LS SE Diff. to Placebo [2]		6.0687		
95% CI [2]		13.225, 37.289		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.98 [0.465, 1.504]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 11				
n (%)	34 (48.6)	33 (47.1)	26 (36.1)	26 (36.1)
Mean	43.1	29.3	14.1	10.3
SD	35.32	41.46	28.55	26.28
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 100	-33, 100
LS Mean [2]		28.444		7.778
LS SE [2]		5.1393		5.4959
95% CI [2]		18.248, 38.640		-3.125, 18.681
LS Mean Diff. to Placebo [2]		20.666		
LS SE Diff. to Placebo [2]		7.3324		
95% CI [2]		6.101, 35.231		
One-sided p-value [2]		0.0030		
Hedge's G (95% CI)		0.72 [0.186, 1.246]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 12				
n (%)	33 (47.1)	32 (45.7)	24 (33.3)	24 (33.3)
Mean	47.5	34.4	12.5	8.3
SD	35.39	44.39	27.47	28.23
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 100	-33, 100
LS Mean [2]		33.925		3.087
LS SE [2]		4.7593		5.1418
95% CI [2]		24.494, 43.356		-7.101, 13.274
LS Mean Diff. to Placebo [2]		30.838		
LS SE Diff. to Placebo [2]		6.7809		
95% CI [2]		17.388, 44.289		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.18 [0.605, 1.749]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 13				
n (%)	33 (47.1)	32 (45.7)	23 (31.9)	22 (30.6)
Mean	50.5	36.5	10.1	4.5
SD	33.46	35.28	21.17	18.67
Median	66.7	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 67	-33, 67
LS Mean [2]		34.912		4.375
LS SE [2]		4.0189		4.4443
95% CI [2]		26.944, 42.880		-4.432, 13.183
LS Mean Diff. to Placebo [2]		30.536		
LS SE Diff. to Placebo [2]		5.7331		
95% CI [2]		19.158, 41.915		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.39 [0.786, 1.991]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 14				
n (%)	32 (45.7)	31 (44.3)	22 (30.6)	21 (29.2)
Mean	43.8	32.3	19.7	7.9
SD	39.20	39.89	22.20	23.34
Median	50.0	33.3	16.7	0.0
Min, Max	0, 100	-33, 100	0, 67	-33, 67
LS Mean [2]		29.225		8.949
LS SE [2]		4.5771		5.0880
95% CI [2]		20.154, 38.296		-1.133, 19.031
LS Mean Diff. to Placebo [2]		20.276		
LS SE Diff. to Placebo [2]		6.5730		
95% CI [2]		7.237, 33.315		
One-sided p-value [2]		0.0013		
Hedge's G (95% CI)		0.82 [0.247, 1.399]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 15				
n (%)	31 (44.3)	30 (42.9)	23 (31.9)	22 (30.6)
Mean	45.2	31.1	11.6	1.5
SD	38.05	43.71	16.23	19.18
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 33	-33, 33
LS Mean [2]		31.724		0.252
LS SE [2]		4.5194		4.9359
95% CI [2]		22.766, 40.683		-9.532, 10.036
LS Mean Diff. to Placebo [2]		31.473		
LS SE Diff. to Placebo [2]		6.4204		
95% CI [2]		18.730, 44.215		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.31 [0.702, 1.911]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	20 (27.8)
Mean	43.1	29.4	16.7	8.3
SD	38.95	39.15	25.36	23.88
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 67	-33, 67
LS Mean [2]		28.728		7.091
LS SE [2]		4.6289		5.3561
95% CI [2]		19.551, 37.906		-3.525, 17.707
LS Mean Diff. to Placebo [2]		21.637		
LS SE Diff. to Placebo [2]		6.8374		
95% CI [2]		8.073, 35.202		
One-sided p-value [2]		0.0010		
Hedge's G (95% CI)		0.83 [0.260, 1.409]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 17				
n (%)	32 (45.7)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	42.7	29.0	14.0	5.3
SD	36.15	40.13	20.23	20.07
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 67	-33, 67
LS Mean [2]		32.838		6.282
LS SE [2]		4.8424		5.5905
95% CI [2]		23.221, 42.455		-4.826, 17.390
LS Mean Diff. to Placebo [2]		26.556		
LS SE Diff. to Placebo [2]		7.1595		
95% CI [2]		12.321, 40.792		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		1.02 [0.416, 1.626]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 18				
n (%)	33 (47.1)	32 (45.7)	20 (27.8)	19 (26.4)
Mean	51.5	37.5	8.3	1.8
SD	36.41	37.63	14.81	17.48
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 33	-33, 33
LS Mean [2]		36.933		-1.895
LS SE [2]		4.3741		5.0996
95% CI [2]		28.258, 45.608		-12.011, 8.221
LS Mean Diff. to Placebo [2]		38.829		
LS SE Diff. to Placebo [2]		6.4844		
95% CI [2]		25.952, 51.705		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.63 [0.978, 2.278]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 19				
n (%)	33 (47.1)	32 (45.7)	18 (25.0)	17 (23.6)
Mean	40.4	28.1	9.3	0.0
SD	37.04	40.70	19.15	16.67
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 67	-33, 33
LS Mean [2]		28.894		0.348
LS SE [2]		4.4904		5.4546
95% CI [2]		19.981, 37.807		-10.479, 11.175
LS Mean Diff. to Placebo [2]		28.546		
LS SE Diff. to Placebo [2]		6.8454		
95% CI [2]		14.946, 42.146		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.15 [0.518, 1.780]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 20				
n (%)	30 (42.9)	29 (41.4)	16 (22.2)	16 (22.2)
Mean	41.1	29.9	16.7	12.5
SD	38.84	40.18	29.81	31.91
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-33, 100	0, 100	-33, 100
LS Mean [2]		27.545		5.346
LS SE [2]		5.5662		6.9186
95% CI [2]		16.478, 38.612		-8.415, 19.107
LS Mean Diff. to Placebo [2]		22.198		
LS SE Diff. to Placebo [2]		8.7031		
95% CI [2]		4.875, 39.522		
One-sided p-value [2]		0.0063		
Hedge's G (95% CI)		0.75 [0.117, 1.377]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 21				
n (%)	32 (45.7)	31 (44.3)	14 (19.4)	14 (19.4)
Mean	41.7	28.0	11.9	9.5
SD	38.80	38.58	28.06	30.46
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 100	-33, 100
LS Mean [2]		30.328		4.462
LS SE [2]		5.0519		6.6177
95% CI [2]		20.294, 40.363		-8.681, 17.605
LS Mean Diff. to Placebo [2]		25.866		
LS SE Diff. to Placebo [2]		8.1589		
95% CI [2]		9.646, 42.086		
One-sided p-value [2]		0.0011		
Hedge's G (95% CI)		0.94 [0.276, 1.596]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 22				
n (%)	31 (44.3)	30 (42.9)	19 (26.4)	19 (26.4)
Mean	39.8	25.6	7.0	0.0
SD	33.80	41.69	17.84	19.25
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 67	-33, 67
LS Mean [2]		28.451		-0.890
LS SE [2]		4.5095		5.3183
95% CI [2]		19.498, 37.404		-11.452, 9.672
LS Mean Diff. to Placebo [2]		29.341		
LS SE Diff. to Placebo [2]		6.7475		
95% CI [2]		15.928, 42.754		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.20 [0.575, 1.818]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 23				
n (%)	29 (41.4)	28 (40.0)	13 (18.1)	13 (18.1)
Mean	40.2	28.6	10.3	2.6
SD	37.14	43.24	21.01	25.32
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	-67, 100	0, 67	-33, 67
LS Mean [2]		27.518		3.502
LS SE [2]		4.9194		6.4362
95% CI [2]		17.737, 37.300		-9.305, 16.309
LS Mean Diff. to Placebo [2]		24.016		
LS SE Diff. to Placebo [2]		7.9065		
95% CI [2]		8.273, 39.760		
One-sided p-value [2]		0.0016		
Hedge's G (95% CI)		0.93 [0.247, 1.623]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	36.5	23.8	6.1	0.0
SD	39.31	41.02	13.48	14.91
Median	33.3	0.0	0.0	0.0
Min, Max	0, 100	-67, 100	0, 33	-33, 33
LS Mean [2]		22.664		1.668
LS SE [2]		4.9772		6.4447
95% CI [2]		12.720, 32.607		-11.221, 14.557
LS Mean Diff. to Placebo [2]		20.995		
LS SE Diff. to Placebo [2]		7.9789		
95% CI [2]		5.026, 36.965		
One-sided p-value [2]		0.0054		
Hedge's G (95% CI)		0.92 [0.153, 1.679]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	29.8	21.1	13.3	6.7
SD	31.22	22.80	18.26	14.91
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	0, 67	0, 33	0, 33
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	39.4	24.2	22.2	16.7
SD	29.13	21.56	17.21	18.26
Median	33.3	33.3	33.3	16.7
Min, Max	0, 100	0, 67	0, 33	0, 33

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	36.1	25.0	25.0	25.0
SD	26.43	20.72	31.91	31.91
Median	33.3	33.3	16.7	16.7
Min, Max	0, 67	0, 67	0, 67	0, 67
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	41.7	27.8	0.0	0.0
SD	35.18	27.83	0.00	0.00
Median	50.0	33.3	0.0	0.0
Min, Max	0, 100	0, 67	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated improvement of GHS and functioning scores but worsening for symptom scales. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo for GHS and functioning scales and favored placebo over Nirogacestat for symptom scores.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	33.3	24.2	11.1	11.1
SD	33.33	21.56	19.25	19.25
Median	33.3	33.3	0.0	0.0
Min, Max	0, 100	0, 67	0, 33	0, 33
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	20.8	8.3	33.3	33.3
SD	17.25	23.57	38.49	38.49
Median	33.3	0.0	33.3	33.3
Min, Max	0, 33	-33, 33	0, 67	0, 67

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 31				
n (%)	6 (8.6)	6 (8.6)	4 (5.6)	4 (5.6)
Mean	33.3	22.2	16.7	16.7
SD	29.81	17.21	33.33	33.33
Median	33.3	33.3	0.0	0.0
Min, Max	0, 67	0, 33	0, 67	0, 67
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	16.7	11.1	0.0	0.0
SD	27.89	17.21	0.00	0.00
Median	0.0	0.0	0.0	0.0
Min, Max	0, 67	0, 33	0, 0	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Diarrhoea				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	26.7	20.0		
SD	43.46	29.81		
Median	0.0	0.0		
Min, Max	0, 100	0, 67		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS = Global Health Score; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.4.1
Summary and Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double-Blind Phase
Global Health Score/Quality of Life and Domain Scores
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Diarrhoea				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	66.7	-33.3		
SD	NA	NA		
Median	66.7	-33.3		
Min, Max	67, 67	-33, -33		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	14.3	4.8	0.0	-33.3
SD	26.23	29.99	NA	NA
Median	0.0	0.0	0.0	-33.3
Min, Max	0, 67	-33, 67	0, 0	-33, -33

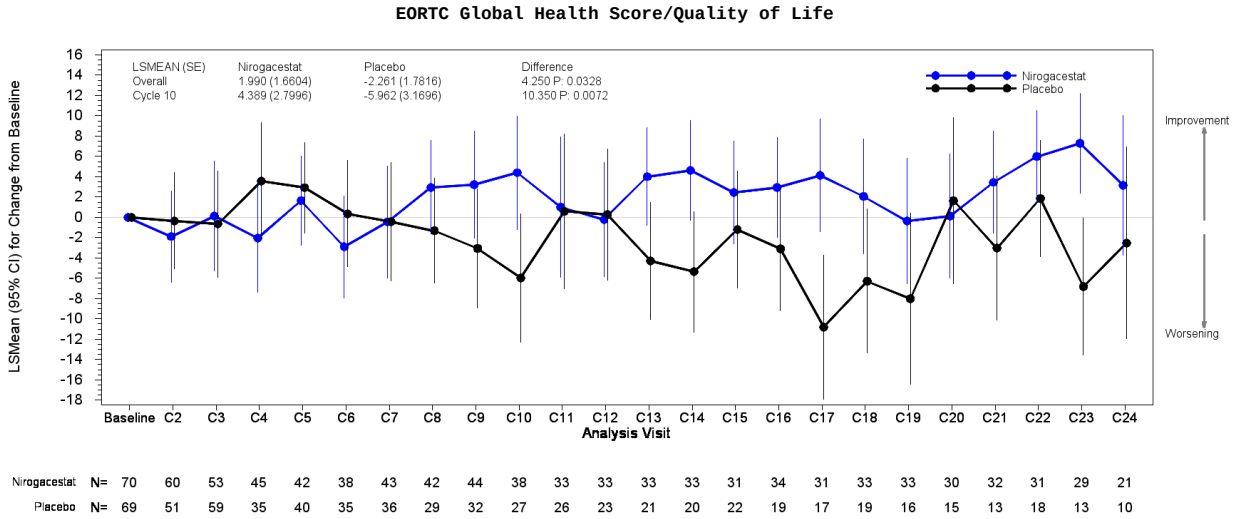
Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline EORTC QLQ-C30 score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (GHS, Role Functioning, Pain, Emotional Functioning Scale, Cognitive Functioning Scale, Social Functioning Scale, Fatigue, Nausea and Vomiting, Dyspnoea, Insomnia, Appetite Loss, Constipation and Diarrhoea) or a heterogenous autoregressive 1 (Physical Functioning) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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1.2.2 Figure MMRM EORTC QLQ-C30

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2025_GBA

Figure 64.4.2
Mixed Model Repeated Measures: Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double Blind Phase
Intent-to-Treat Population

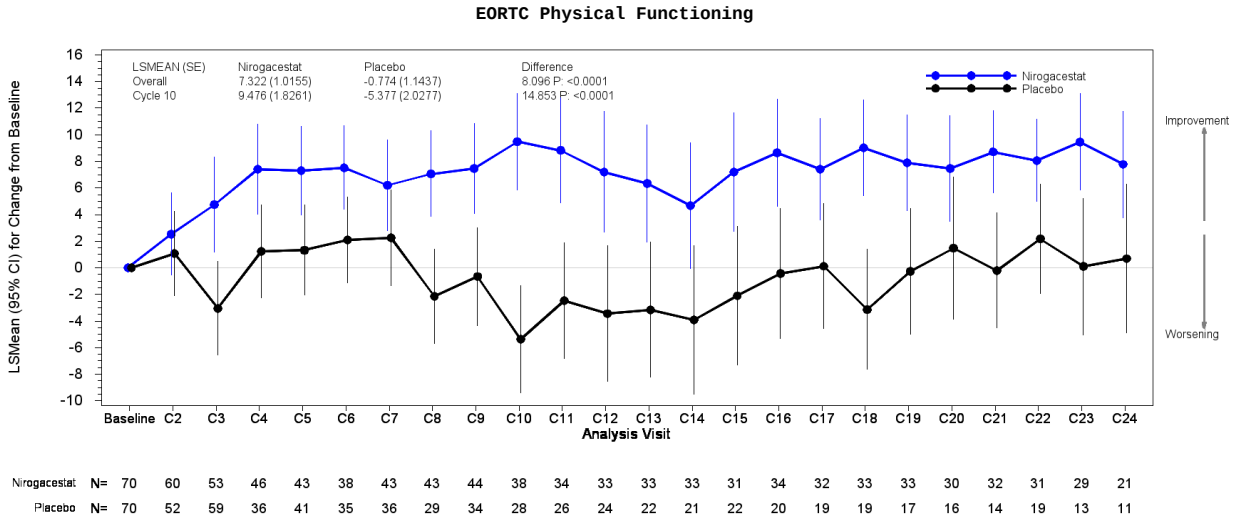


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

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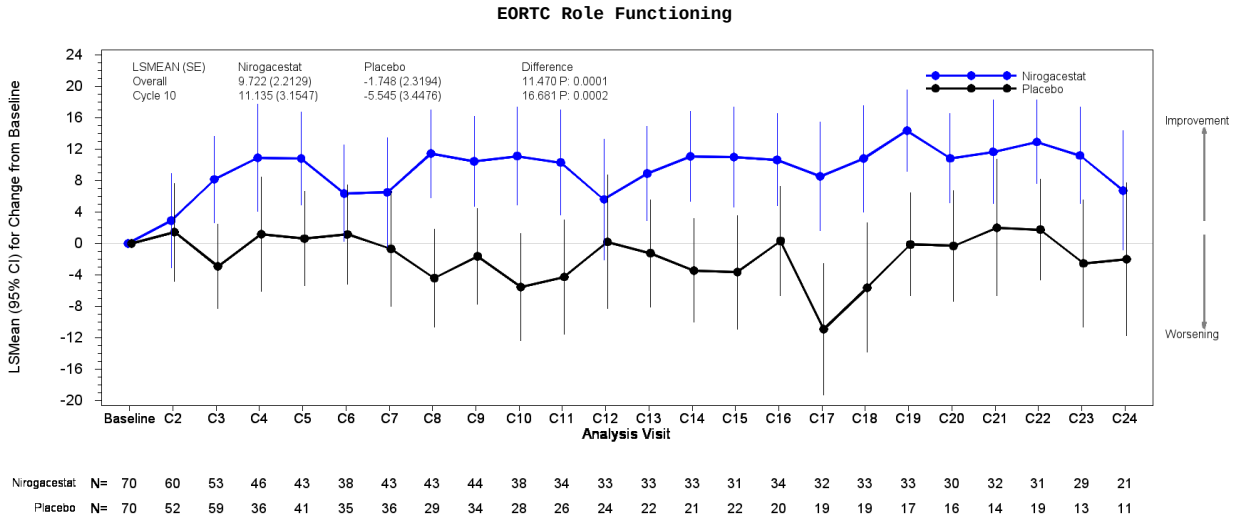
Figure 64.4.2
Mixed Model Repeated Measures: Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

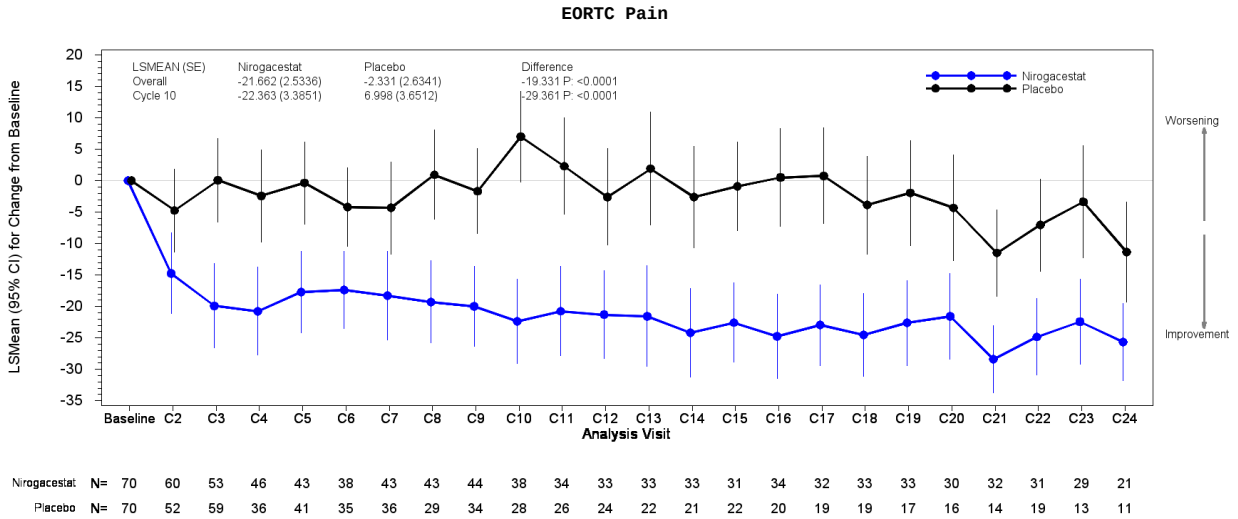
Figure 64.4.2
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Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

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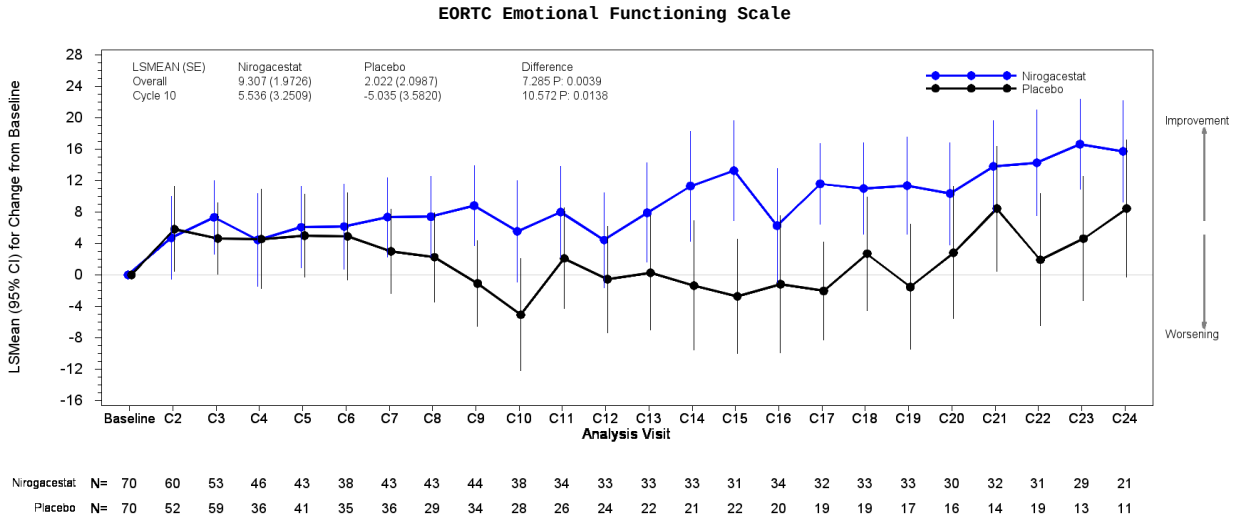
Figure 64.4.2
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Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

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Intent-to-Treat Population

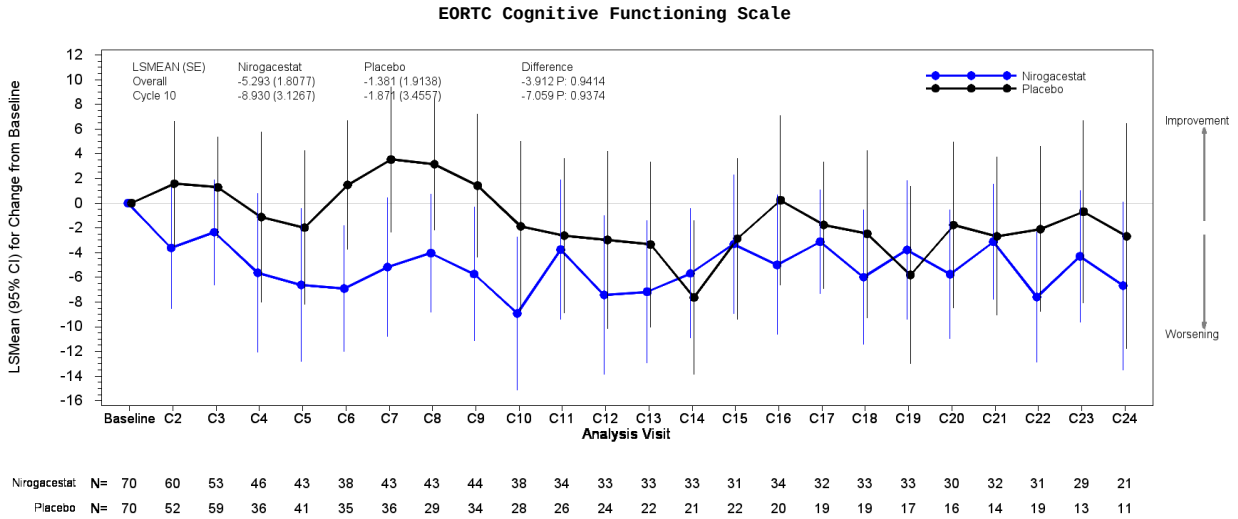


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

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Figure 64.4.2
Mixed Model Repeated Measures: Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double Blind Phase
Intent-to-Treat Population

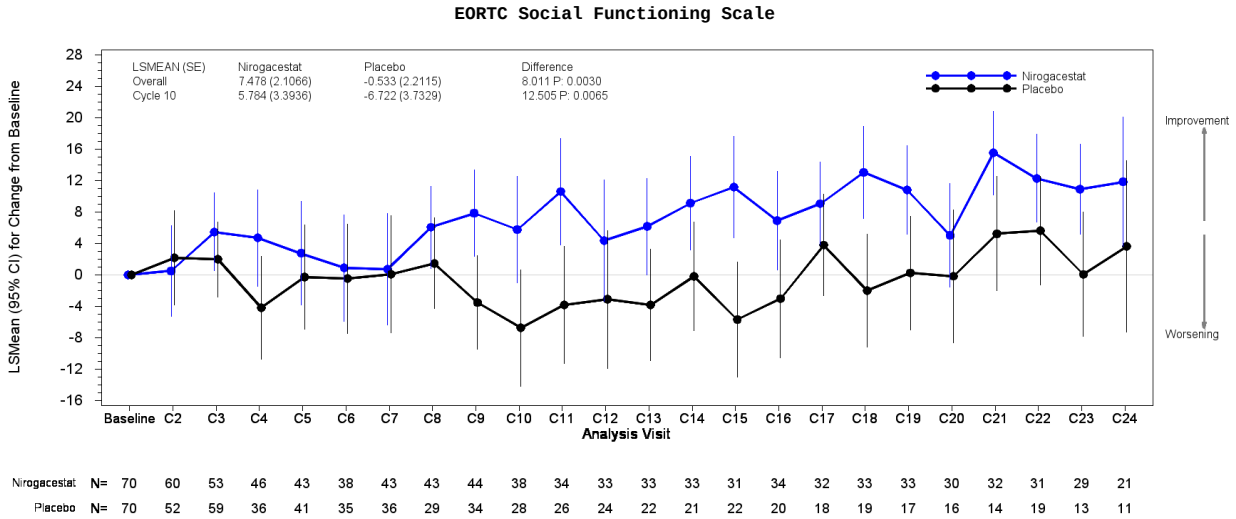


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

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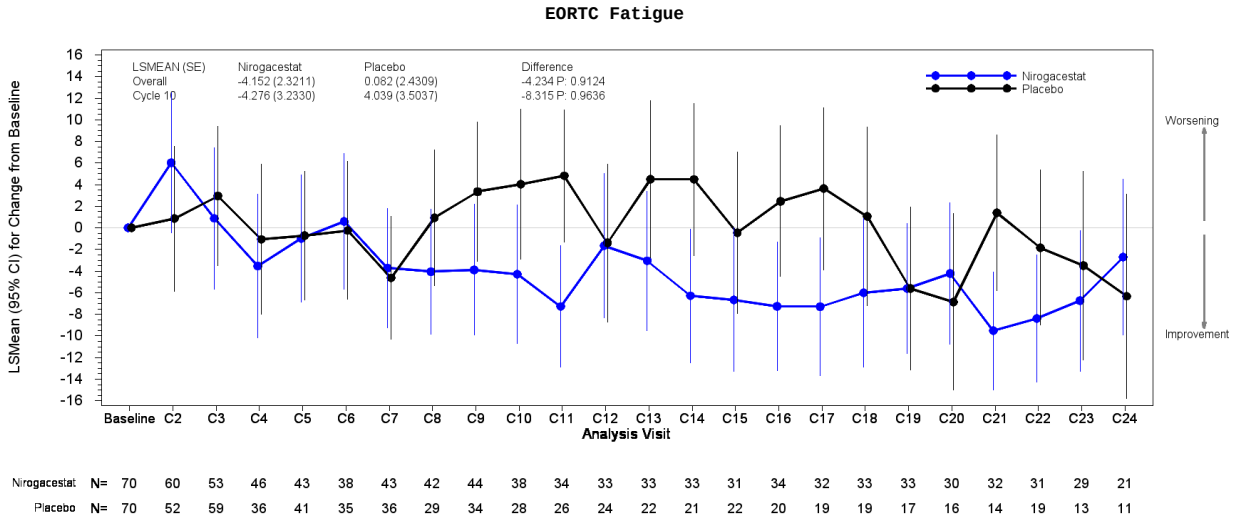
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Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

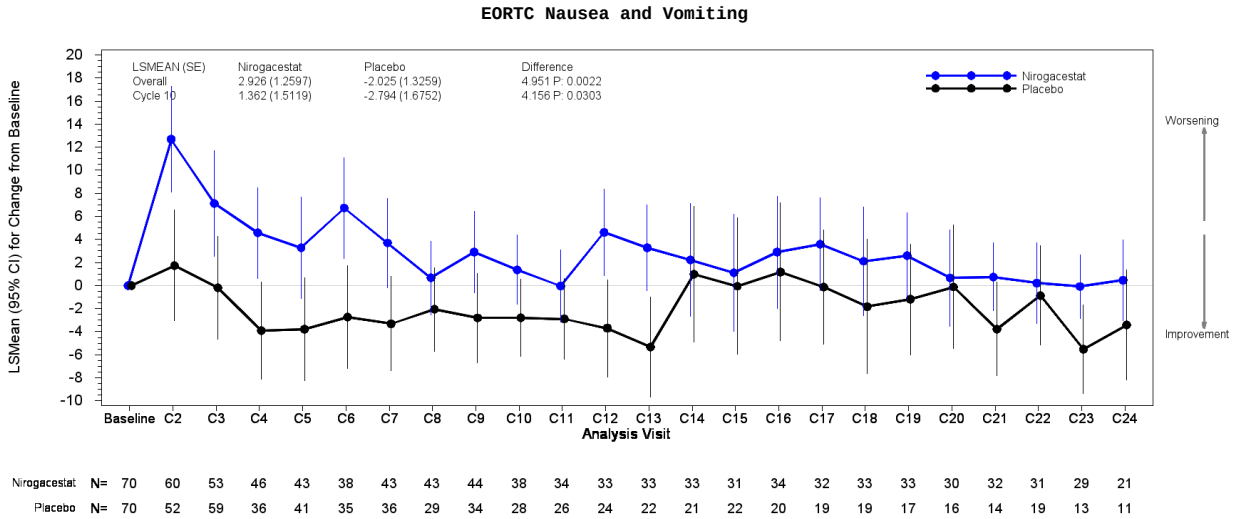
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Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

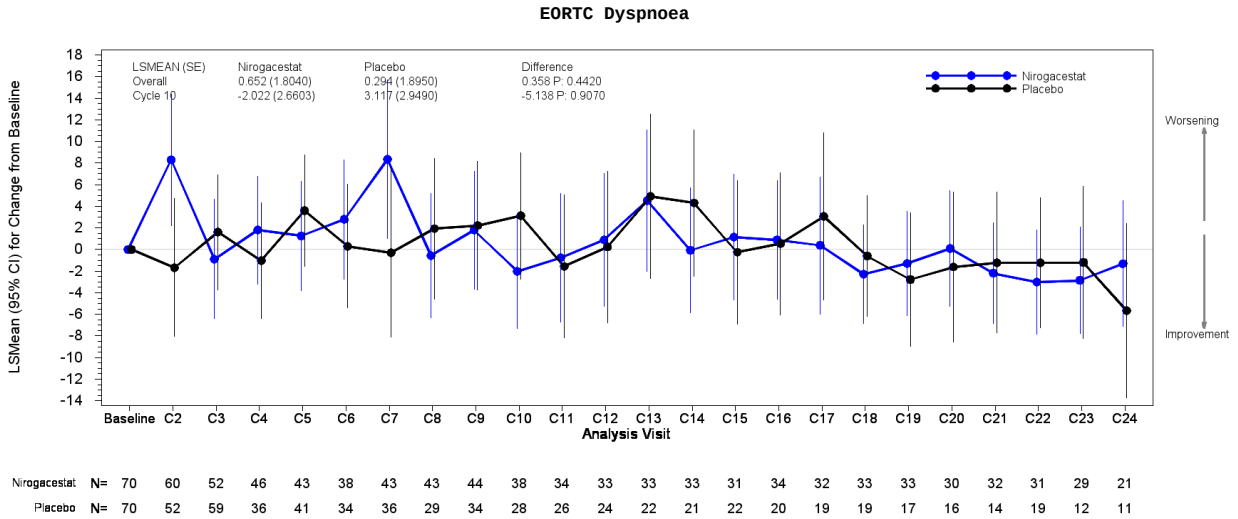
Figure 64.4.2
Mixed Model Repeated Measures: Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

Figure 64.4.2
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Intent-to-Treat Population

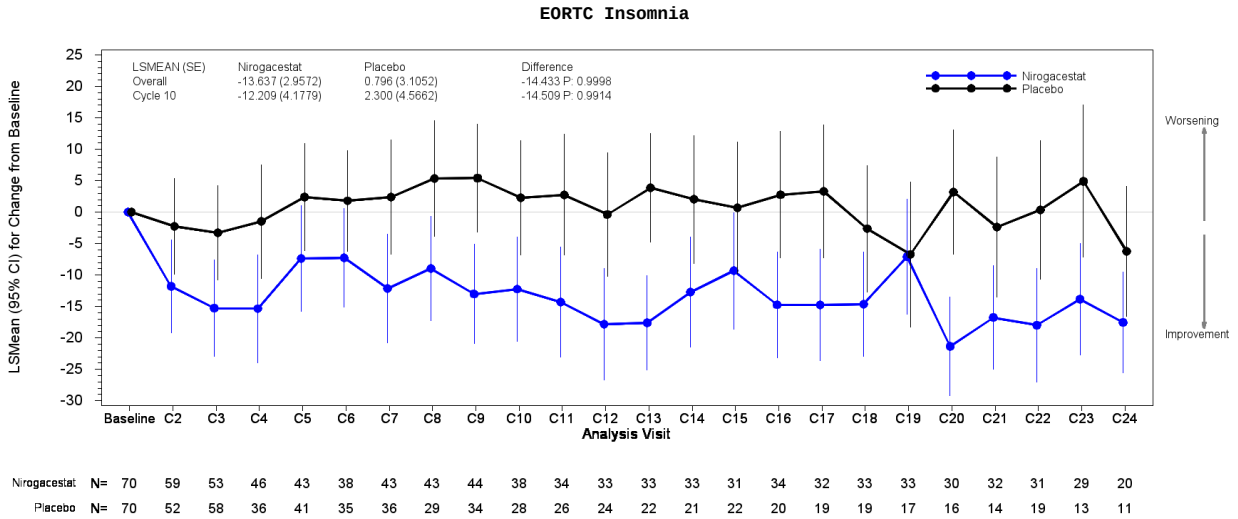


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

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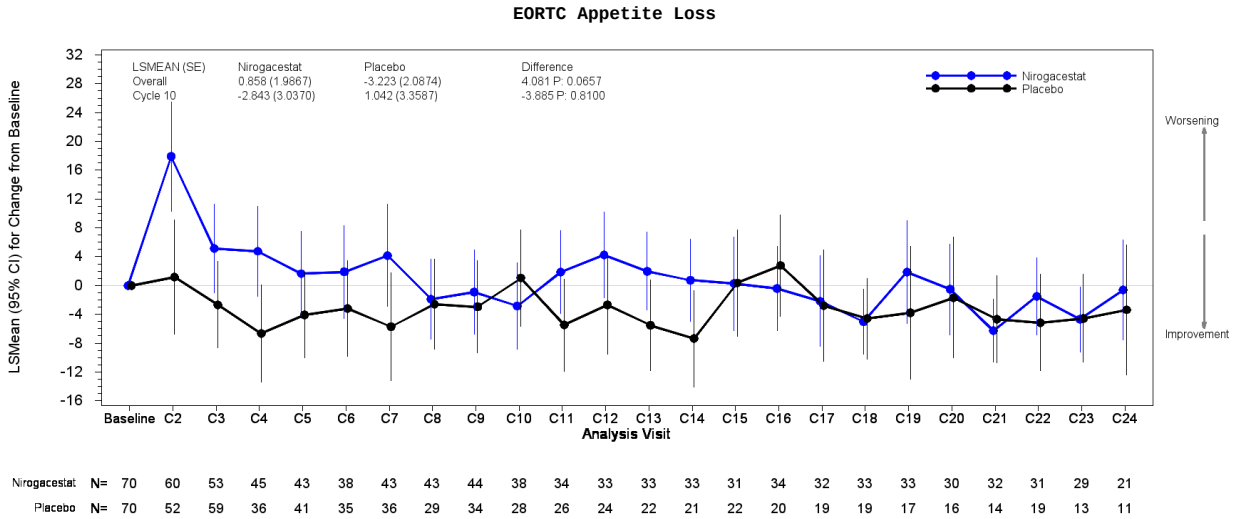
Figure 64.4.2
Mixed Model Repeated Measures: Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

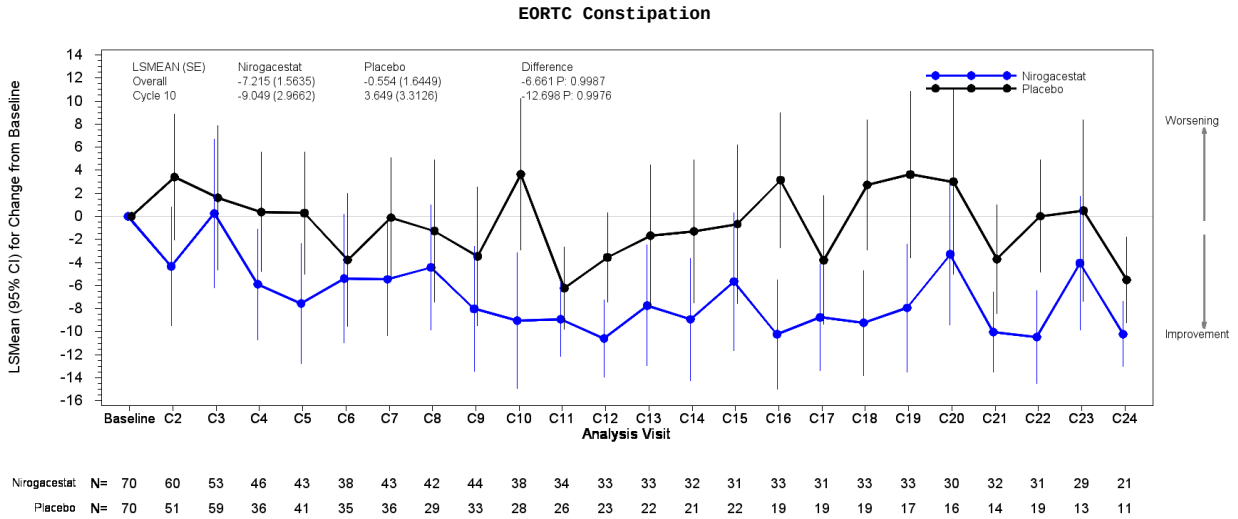
Figure 64.4.2
Mixed Model Repeated Measures: Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

Figure 64.4.2
Mixed Model Repeated Measures: Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double Blind Phase
Intent-to-Treat Population

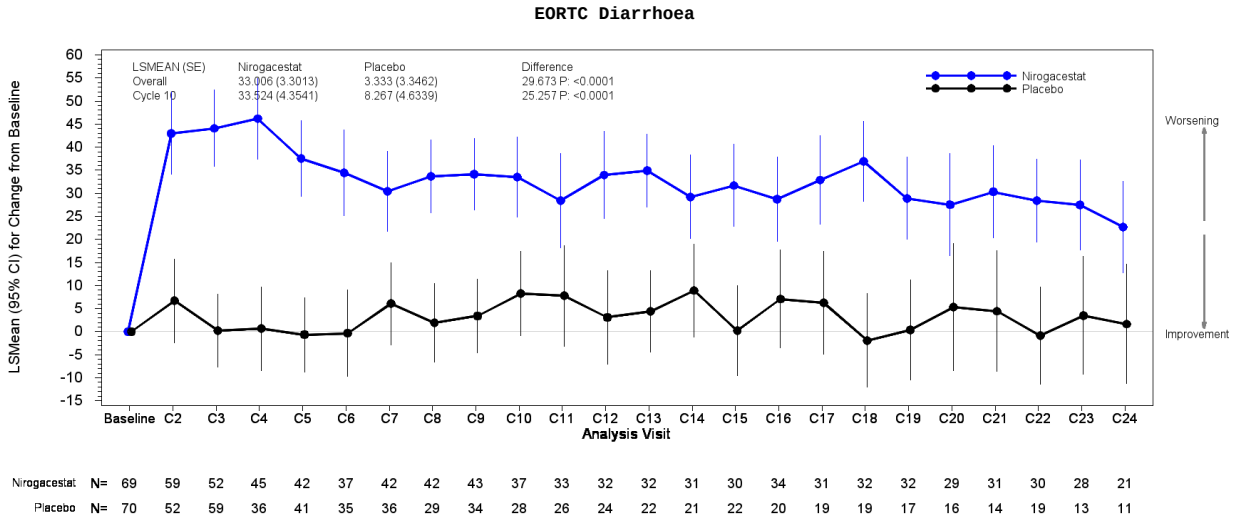


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

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Figure 64.4.2
Mixed Model Repeated Measures: Change from Baseline in EORTC QLQ-C30 Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.4.1, Dataset(s): ADSL, ADQS

1.3 GODDESS DTIS

1.3.1 Table MMRM DTIS

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	2.8		2.7	
SD	1.13		1.24	
Median	2.7		2.8	
Min, Max	1, 5		1, 5	
Effect over Study Duration				
n (%)		68 (97.1)		68 (94.4)
LS Mean [2]		-0.590		0.022
LS SE [2]		0.0751		0.0784
95% CI [2]		-0.738, -0.441		-0.133, 0.177
LS Mean Diff. to Placebo [2]		-0.612		
LS SE Diff. to Placebo [2]		0.1014		
95% CI [2]		-0.812, -0.411		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.97 [-1.322, -0.611]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	55 (76.4)	54 (75.0)
Mean	2.4	-0.4	2.6	0.0
SD	1.15	0.66	1.20	0.60
Median	2.2	-0.4	2.6	0.0
Min, Max	1, 5	-2, 2	1, 5	-3, 1
LS Mean [2]		-0.360		0.014
LS SE [2]		0.0903		0.0915
95% CI [2]		-0.538, -0.181		-0.167, 0.195
LS Mean Diff. to Placebo [2]		-0.373		
LS SE Diff. to Placebo [2]		0.1227		
95% CI [2]		-0.616, -0.131		
One-sided p-value [2]		0.0014		
Hedge's G (95% CI)		-0.54 [-0.918, -0.170]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	60 (83.3)	60 (83.3)
Mean	2.2	-0.6	2.7	0.0
SD	1.07	0.67	1.14	0.55
Median	1.8	-0.4	2.8	0.0
Min, Max	1, 5	-2, 1	1, 5	-2, 1
LS Mean [2]		-0.486		0.074
LS SE [2]		0.0824		0.0802
95% CI [2]		-0.649, -0.323		-0.084, 0.233
LS Mean Diff. to Placebo [2]		-0.561		
LS SE Diff. to Placebo [2]		0.1083		
95% CI [2]		-0.775, -0.346		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.92 [-1.305, -0.529]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	1.9	-0.6	2.7	0.1
SD	0.90	0.65	1.21	0.59
Median	1.6	-0.6	2.8	0.0
Min, Max	1, 5	-2, 1	1, 5	-2, 1
LS Mean [2]		-0.563		0.023
LS SE [2]		0.0920		0.0954
95% CI [2]		-0.746, -0.381		-0.166, 0.212
LS Mean Diff. to Placebo [2]		-0.586		
LS SE Diff. to Placebo [2]		0.1266		
95% CI [2]		-0.837, -0.335		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.97 [-1.434, -0.512]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	43 (59.7)	42 (58.3)
Mean	2.2	-0.5	2.5	0.0
SD	1.03	0.71	1.17	0.56
Median	2.0	-0.4	2.2	0.0
Min, Max	1, 5	-2, 1	1, 5	-2, 1
LS Mean [2]		-0.440		-0.015
LS SE [2]		0.1012		0.1017
95% CI [2]		-0.641, -0.239		-0.217, 0.187
LS Mean Diff. to Placebo [2]		-0.425		
LS SE Diff. to Placebo [2]		0.1380		
95% CI [2]		-0.699, -0.151		
One-sided p-value [2]		0.0014		
Hedge's G (95% CI)		-0.64 [-1.078, -0.206]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	2.0	-0.5	2.5	0.0
SD	1.00	0.72	1.14	0.36
Median	1.8	-0.3	2.5	0.0
Min, Max	1, 5	-2, 1	1, 5	-1, 1
LS Mean [2]		-0.502		-0.027
LS SE [2]		0.0832		0.0847
95% CI [2]		-0.667, -0.337		-0.195, 0.141
LS Mean Diff. to Placebo [2]		-0.475		
LS SE Diff. to Placebo [2]		0.1121		
95% CI [2]		-0.698, -0.253		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.94 [-1.420, -0.453]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 7				
n (%)	44 (62.9)	44 (62.9)	37 (51.4)	36 (50.0)
Mean	2.1	-0.7	2.5	-0.1
SD	1.20	0.80	1.16	0.51
Median	1.6	-0.5	2.2	0.0
Min, Max	1, 5	-3, 1	1, 5	-2, 1
LS Mean [2]		-0.536		-0.053
LS SE [2]		0.0936		0.0973
95% CI [2]		-0.721, -0.351		-0.246, 0.139
LS Mean Diff. to Placebo [2]		-0.483		
LS SE Diff. to Placebo [2]		0.1292		
95% CI [2]		-0.739, -0.227		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		-0.80 [-1.256, -0.341]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	31 (43.1)	30 (41.7)
Mean	2.3	-0.5	2.8	0.0
SD	1.15	0.81	1.11	0.47
Median	2.0	-0.4	2.8	0.0
Min, Max	1, 5	-3, 1	1, 5	-1, 1
LS Mean [2]		-0.439		0.009
LS SE [2]		0.0956		0.1025
95% CI [2]		-0.629, -0.250		-0.194, 0.212
LS Mean Diff. to Placebo [2]		-0.448		
LS SE Diff. to Placebo [2]		0.1345		
95% CI [2]		-0.715, -0.181		
One-sided p-value [2]		0.0006		
Hedge's G (95% CI)		-0.75 [-1.227, -0.264]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	2.0	-0.7	2.7	0.1
SD	1.03	0.73	1.19	0.48
Median	1.6	-0.4	2.6	0.1
Min, Max	1, 5	-2, 0	1, 5	-1, 1
LS Mean [2]		-0.582		0.040
LS SE [2]		0.0836		0.0881
95% CI [2]		-0.748, -0.417		-0.135, 0.214
LS Mean Diff. to Placebo [2]		-0.622		
LS SE Diff. to Placebo [2]		0.1149		
95% CI [2]		-0.850, -0.394		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.16 [-1.641, -0.675]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 10				
n (%)	39 (55.7)	39 (55.7)	28 (38.9)	28 (38.9)
Mean	1.9	-0.8	2.9	0.2
SD	1.07	0.81	1.22	0.53
Median	1.6	-0.6	3.0	0.2
Min, Max	1, 5	-3, 0	1, 5	-1, 2
LS Mean [2]		-0.634		0.091
LS SE [2]		0.0947		0.1021
95% CI [2]		-0.822, -0.447		-0.112, 0.293
LS Mean Diff. to Placebo [2]		-0.725		
LS SE Diff. to Placebo [2]		0.1336		
95% CI [2]		-0.990, -0.460		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.27 [-1.802, -0.740]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 11				
n (%)	35 (50.0)	35 (50.0)	26 (36.1)	26 (36.1)
Mean	1.9	-0.8	2.8	0.2
SD	1.02	0.86	1.06	0.49
Median	1.4	-0.6	2.9	0.2
Min, Max	1, 5	-3, 1	1, 4	-1, 2
LS Mean [2]		-0.670		0.096
LS SE [2]		0.0992		0.1072
95% CI [2]		-0.866, -0.473		-0.117, 0.308
LS Mean Diff. to Placebo [2]		-0.765		
LS SE Diff. to Placebo [2]		0.1407		
95% CI [2]		-1.044, -0.486		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.34 [-1.902, -0.781]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 12				
n (%)	35 (50.0)	35 (50.0)	24 (33.3)	24 (33.3)
Mean	2.1	-0.7	2.5	0.1
SD	1.10	0.86	1.26	0.57
Median	1.8	-0.6	2.2	0.2
Min, Max	1, 5	-3, 1	1, 5	-2, 1
LS Mean [2]		-0.560		0.021
LS SE [2]		0.0996		0.1095
95% CI [2]		-0.757, -0.362		-0.196, 0.238
LS Mean Diff. to Placebo [2]		-0.581		
LS SE Diff. to Placebo [2]		0.1431		
95% CI [2]		-0.865, -0.297		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.02 [-1.573, -0.470]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 13				
n (%)	34 (48.6)	34 (48.6)	23 (31.9)	22 (30.6)
Mean	2.1	-0.7	2.9	0.2
SD	1.14	0.78	1.25	0.66
Median	1.6	-0.7	3.0	0.1
Min, Max	1, 5	-3, 0	1, 5	-1, 2
LS Mean [2]		-0.607		0.182
LS SE [2]		0.1094		0.1226
95% CI [2]		-0.824, -0.390		-0.061, 0.425
LS Mean Diff. to Placebo [2]		-0.789		
LS SE Diff. to Placebo [2]		0.1596		
95% CI [2]		-1.106, -0.472		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.28 [-1.871, -0.698]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	1.9	-0.7	2.9	0.1
SD	1.04	0.78	1.31	0.44
Median	1.6	-0.6	2.9	0.2
Min, Max	1, 4	-2, 1	1, 5	-1, 1
LS Mean [2]		-0.543		0.183
LS SE [2]		0.0966		0.1089
95% CI [2]		-0.735, -0.352		-0.033, 0.398
LS Mean Diff. to Placebo [2]		-0.726		
LS SE Diff. to Placebo [2]		0.1404		
95% CI [2]		-1.005, -0.447		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.36 [-1.963, -0.755]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	2.1	-0.7	2.8	0.0
SD	1.13	0.84	1.20	0.57
Median	1.8	-0.8	3.0	0.0
Min, Max	1, 5	-3, 1	1, 5	-1, 2
LS Mean [2]		-0.581		0.053
LS SE [2]		0.1024		0.1135
95% CI [2]		-0.784, -0.378		-0.172, 0.278
LS Mean Diff. to Placebo [2]		-0.633		
LS SE Diff. to Placebo [2]		0.1478		
95% CI [2]		-0.927, -0.340		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.14 [-1.730, -0.554]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	21 (29.2)	21 (29.2)
Mean	1.9	-0.7	2.8	0.1
SD	1.02	0.82	1.27	0.61
Median	1.7	-0.6	2.8	0.0
Min, Max	1, 5	-3, 0	1, 5	-1, 1
LS Mean [2]		-0.635		0.127
LS SE [2]		0.1111		0.1273
95% CI [2]		-0.856, -0.414		-0.126, 0.380
LS Mean Diff. to Placebo [2]		-0.762		
LS SE Diff. to Placebo [2]		0.1643		
95% CI [2]		-1.088, -0.436		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.22 [-1.810, -0.631]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	2.0	-0.8	2.5	0.1
SD	1.03	0.83	1.33	0.70
Median	1.8	-0.8	2.2	0.2
Min, Max	1, 5	-2, 1	1, 5	-2, 1
LS Mean [2]		-0.666		0.053
LS SE [2]		0.1013		0.1183
95% CI [2]		-0.867, -0.465		-0.181, 0.288
LS Mean Diff. to Placebo [2]		-0.719		
LS SE Diff. to Placebo [2]		0.1514		
95% CI [2]		-1.020, -0.419		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.30 [-1.923, -0.680]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	20 (27.8)
Mean	2.0	-0.8	2.7	0.3
SD	1.05	0.79	1.35	0.68
Median	1.6	-0.8	2.6	0.2
Min, Max	1, 5	-3, 0	1, 5	-1, 2
LS Mean [2]		-0.663		0.153
LS SE [2]		0.1033		0.1208
95% CI [2]		-0.867, -0.458		-0.086, 0.392
LS Mean Diff. to Placebo [2]		-0.816		
LS SE Diff. to Placebo [2]		0.1545		
95% CI [2]		-1.122, -0.509		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.42 [-2.038, -0.803]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	19 (26.4)
Mean	1.9	-0.8	2.4	-0.1
SD	0.90	0.81	1.03	0.75
Median	1.6	-0.8	2.2	-0.2
Min, Max	1, 4	-3, 1	1, 4	-2, 1
LS Mean [2]		-0.666		-0.102
LS SE [2]		0.0931		0.1122
95% CI [2]		-0.851, -0.482		-0.325, 0.120
LS Mean Diff. to Placebo [2]		-0.564		
LS SE Diff. to Placebo [2]		0.1407		
95% CI [2]		-0.843, -0.285		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.08 [-1.673, -0.478]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	2.0	-0.8	2.3	-0.2
SD	1.02	0.84	1.08	0.93
Median	1.7	-0.8	2.0	0.0
Min, Max	1, 4	-3, 1	1, 5	-3, 1
LS Mean [2]		-0.667		-0.200
LS SE [2]		0.1015		0.1250
95% CI [2]		-0.868, -0.466		-0.448, 0.048
LS Mean Diff. to Placebo [2]		-0.467		
LS SE Diff. to Placebo [2]		0.1567		
95% CI [2]		-0.778, -0.156		
One-sided p-value [2]		0.0018		
Hedge's G (95% CI)		-0.85 [-1.485, -0.223]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	15 (20.8)	15 (20.8)
Mean	2.0	-0.9	2.4	-0.1
SD	0.98	0.87	1.16	1.02
Median	1.7	-0.8	2.0	0.0
Min, Max	1, 4	-2, 1	1, 5	-3, 1
LS Mean [2]		-0.619		-0.039
LS SE [2]		0.0994		0.1260
95% CI [2]		-0.816, -0.422		-0.288, 0.211
LS Mean Diff. to Placebo [2]		-0.581		
LS SE Diff. to Placebo [2]		0.1563		
95% CI [2]		-0.890, -0.271		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-1.06 [-1.706, -0.407]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Physical Functioning Score				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	1.9	-0.9	2.3	-0.1
SD	1.00	0.96	1.17	0.86
Median	1.6	-1.2	2.0	0.0
Min, Max	1, 4	-3, 1	1, 5	-3, 1
LS Mean [2]		-0.728		-0.074
LS SE [2]		0.1030		0.1252
95% CI [2]		-0.932, -0.524		-0.322, 0.174
LS Mean Diff. to Placebo [2]		-0.654		
LS SE Diff. to Placebo [2]		0.1583		
95% CI [2]		-0.968, -0.340		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.16 [-1.776, -0.546]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	14 (19.4)	14 (19.4)
Mean	2.1	-0.8	2.5	0.0
SD	1.04	0.86	1.23	0.90
Median	2.0	-1.0	2.4	0.1
Min, Max	1, 4	-3, 1	1, 5	-3, 1
LS Mean [2]		-0.672		-0.031
LS SE [2]		0.0999		0.1286
95% CI [2]		-0.870, -0.474		-0.286, 0.224
LS Mean Diff. to Placebo [2]		-0.641		
LS SE Diff. to Placebo [2]		0.1589		
95% CI [2]		-0.956, -0.326		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.21 [-1.896, -0.522]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	1.7	-0.8	2.7	0.1
SD	0.97	0.77	1.24	1.02
Median	1.2	-0.6	2.6	0.2
Min, Max	1, 4	-2, 0	1, 5	-3, 1
LS Mean [2]		-0.746		-0.071
LS SE [2]		0.1079		0.1393
95% CI [2]		-0.960, -0.531		-0.348, 0.206
LS Mean Diff. to Placebo [2]		-0.675		
LS SE Diff. to Placebo [2]		0.1724		
95% CI [2]		-1.018, -0.331		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.36 [-2.161, -0.557]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	1.7	-0.8	3.5	0.3
SD	0.91	0.87	1.27	0.44
Median	1.0	-0.6	3.6	0.2
Min, Max	1, 4	-3, 0	2, 5	0, 1
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	1.8	-0.7	2.9	0.1
SD	0.94	1.02	1.55	0.41
Median	1.6	-0.2	3.0	0.1
Min, Max	1, 4	-2, 1	1, 5	0, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	2.0	-0.8	2.9	-0.1
SD	1.04	0.72	1.47	0.35
Median	1.8	-0.7	2.8	-0.2
Min, Max	1, 4	-2, 0	1, 5	0, 0
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	1.9	-0.8	3.3	0.6
SD	0.94	0.74	1.56	0.00
Median	1.6	-0.7	3.3	0.6
Min, Max	1, 4	-2, 0	2, 4	1, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 29				
n (%)	12 (17.1)	12 (17.1)	3 (4.2)	3 (4.2)
Mean	2.2	-0.8	3.0	0.4
SD	0.81	0.88	0.69	0.53
Median	2.2	-0.7	2.6	0.2
Min, Max	1, 4	-3, 0	3, 4	0, 1
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	2.2	-1.1	2.9	-0.4
SD	0.90	0.76	1.27	1.47
Median	2.1	-1.1	2.8	0.0
Min, Max	1, 4	-2, 0	1, 4	-2, 1

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	5 (6.9)	5 (6.9)
Mean	2.0	-1.0	2.6	-0.2
SD	0.57	1.06	0.91	1.04
Median	1.8	-1.0	2.6	0.2
Min, Max	1, 3	-3, 0	2, 4	-2, 1
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	2.3	-1.3	2.0	0.5
SD	0.65	0.91	0.57	0.42
Median	2.1	-1.3	2.0	0.5
Min, Max	2, 3	-3, 0	2, 2	0, 1

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	2.0	-1.1		
SD	0.79	0.91		
Median	2.0	-1.2		
Min, Max	1, 3	-2, 0		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	1.0	-0.4		
SD	NA	NA		
Median	1.0	-0.4		
Min, Max	1, 1	0, 0		

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Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Physical Functioning Score				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	1.0	-1.2		
SD	NA	NA		
Median	1.0	-1.2		
Min, Max	1, 1	-1, -1		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	1.0	-1.2		
SD	NA	NA		
Median	1.0	-1.2		
Min, Max	1, 1	-1, -1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Physical Functioning Score				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	2.8	-0.4		
SD	NA	NA		
Median	2.8	-0.4		
Min, Max	3, 3	0, 0		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	2.3	-0.5	2.8	0.2
SD	1.16	0.76	NA	NA
Median	1.6	-0.4	2.8	0.2
Min, Max	1, 4	-2, 0	3, 3	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	2.9		2.9	
SD	1.28		1.34	
Median	2.7		2.7	
Min, Max	1, 5		1, 5	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Effect over Study Duration				
n (%)		68 (97.1)		68 (94.4)
LS Mean [2]		-0.603		0.150
LS SE [2]		0.0966		0.1015
95% CI [2]		-0.794, -0.412		-0.050, 0.351
LS Mean Diff. to Placebo [2]		-0.753		
LS SE Diff. to Placebo [2]		0.1299		
95% CI [2]		-1.009, -0.496		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.92 [-1.274, -0.567]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	55 (76.4)	54 (75.0)
Mean	2.4	-0.4	2.8	-0.1
SD	1.20	0.86	1.24	0.68
Median	2.2	-0.3	2.7	0.0
Min, Max	1, 5	-4, 1	1, 5	-2, 2
LS Mean [2]		-0.454		-0.038
LS SE [2]		0.1179		0.1192
95% CI [2]		-0.687, -0.220		-0.274, 0.198
LS Mean Diff. to Placebo [2]		-0.416		
LS SE Diff. to Placebo [2]		0.1595		
95% CI [2]		-0.732, -0.100		
One-sided p-value [2]		0.0052		
Hedge's G (95% CI)		-0.46 [-0.837, -0.092]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	60 (83.3)	60 (83.3)
Mean	2.3	-0.5	2.9	0.1
SD	1.18	1.05	1.28	0.86
Median	2.0	-0.3	3.0	0.0
Min, Max	1, 5	-4, 1	1, 5	-3, 2
LS Mean [2]		-0.558		0.014
LS SE [2]		0.1334		0.1303
95% CI [2]		-0.822, -0.294		-0.244, 0.272
LS Mean Diff. to Placebo [2]		-0.572		
LS SE Diff. to Placebo [2]		0.1789		
95% CI [2]		-0.926, -0.218		
One-sided p-value [2]		0.0009		
Hedge's G (95% CI)		-0.58 [-0.954, -0.200]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	2.2	-0.5	3.1	0.2
SD	1.05	0.88	1.22	0.76
Median	2.0	-0.3	3.3	0.0
Min, Max	1, 5	-4, 1	1, 5	-1, 2
LS Mean [2]		-0.580		0.149
LS SE [2]		0.1240		0.1277
95% CI [2]		-0.825, -0.334		-0.104, 0.402
LS Mean Diff. to Placebo [2]		-0.728		
LS SE Diff. to Placebo [2]		0.1705		
95% CI [2]		-1.066, -0.390		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.90 [-1.357, -0.442]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	43 (59.7)	42 (58.3)
Mean	2.5	-0.4	2.9	0.1
SD	1.18	1.06	1.30	0.71
Median	2.3	0.0	3.0	0.0
Min, Max	1, 5	-4, 1	1, 5	-1, 2
LS Mean [2]		-0.342		0.094
LS SE [2]		0.1309		0.1310
95% CI [2]		-0.601, -0.082		-0.166, 0.353
LS Mean Diff. to Placebo [2]		-0.435		
LS SE Diff. to Placebo [2]		0.1773		
95% CI [2]		-0.787, -0.084		
One-sided p-value [2]		0.0079		
Hedge's G (95% CI)		-0.51 [-0.942, -0.078]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	2.4	-0.2	2.8	0.1
SD	1.13	0.94	1.16	0.79
Median	2.3	0.0	2.5	0.0
Min, Max	1, 5	-2, 2	1, 5	-2, 3
LS Mean [2]		-0.384		0.040
LS SE [2]		0.1228		0.1244
95% CI [2]		-0.628, -0.141		-0.207, 0.286
LS Mean Diff. to Placebo [2]		-0.424		
LS SE Diff. to Placebo [2]		0.1664		
95% CI [2]		-0.754, -0.094		
One-sided p-value [2]		0.0062		
Hedge's G (95% CI)		-0.57 [-1.036, -0.099]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 7				
n (%)	44 (62.9)	44 (62.9)	37 (51.4)	36 (50.0)
Mean	2.4	-0.5	2.9	-0.1
SD	1.25	1.20	1.26	0.89
Median	2.0	0.0	3.0	0.0
Min, Max	1, 5	-4, 2	1, 5	-3, 2
LS Mean [2]		-0.507		0.059
LS SE [2]		0.1417		0.1471
95% CI [2]		-0.787, -0.226		-0.232, 0.350
LS Mean Diff. to Placebo [2]		-0.566		
LS SE Diff. to Placebo [2]		0.1969		
95% CI [2]		-0.956, -0.176		
One-sided p-value [2]		0.0024		
Hedge's G (95% CI)		-0.62 [-1.069, -0.168]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	31 (43.1)	30 (41.7)
Mean	2.5	-0.4	3.2	0.4
SD	1.25	1.15	1.22	0.76
Median	2.0	0.0	3.3	0.3
Min, Max	1, 5	-4, 2	1, 5	-1, 2
LS Mean [2]		-0.508		0.267
LS SE [2]		0.1315		0.1404
95% CI [2]		-0.769, -0.248		-0.011, 0.544
LS Mean Diff. to Placebo [2]		-0.775		
LS SE Diff. to Placebo [2]		0.1849		
95% CI [2]		-1.141, -0.409		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.94 [-1.429, -0.448]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	2.2	-0.7	2.9	0.3
SD	1.11	1.15	1.23	0.91
Median	2.0	-0.3	2.7	0.0
Min, Max	1, 5	-4, 1	1, 5	-1, 4
LS Mean [2]		-0.651		0.091
LS SE [2]		0.1237		0.1303
95% CI [2]		-0.895, -0.406		-0.167, 0.348
LS Mean Diff. to Placebo [2]		-0.742		
LS SE Diff. to Placebo [2]		0.1715		
95% CI [2]		-1.081, -0.402		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.93 [-1.404, -0.462]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 10				
n (%)	39 (55.7)	39 (55.7)	28 (38.9)	28 (38.9)
Mean	2.3	-0.5	3.2	0.2
SD	1.27	1.12	1.14	1.04
Median	2.0	-0.3	3.2	0.0
Min, Max	1, 5	-4, 2	1, 5	-1, 4
LS Mean [2]		-0.606		0.078
LS SE [2]		0.1303		0.1400
95% CI [2]		-0.864, -0.348		-0.199, 0.355
LS Mean Diff. to Placebo [2]		-0.684		
LS SE Diff. to Placebo [2]		0.1836		
95% CI [2]		-1.048, -0.321		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		-0.87 [-1.380, -0.365]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 11				
n (%)	35 (50.0)	35 (50.0)	26 (36.1)	26 (36.1)
Mean	2.1	-0.8	3.3	0.5
SD	0.93	1.22	1.05	0.73
Median	2.0	-0.3	3.3	0.7
Min, Max	1, 4	-4, 2	1, 5	-1, 2
LS Mean [2]		-0.797		0.330
LS SE [2]		0.1223		0.1320
95% CI [2]		-1.039, -0.555		0.069, 0.592
LS Mean Diff. to Placebo [2]		-1.127		
LS SE Diff. to Placebo [2]		0.1716		
95% CI [2]		-1.467, -0.787		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.60 [-2.186, -1.023]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 12				
n (%)	35 (50.0)	35 (50.0)	24 (33.3)	24 (33.3)
Mean	2.2	-0.6	3.0	0.3
SD	1.09	1.18	1.04	0.60
Median	2.0	-0.3	3.0	0.0
Min, Max	1, 5	-4, 2	1, 5	-1, 2
LS Mean [2]		-0.545		0.225
LS SE [2]		0.1196		0.1320
95% CI [2]		-0.782, -0.308		-0.036, 0.487
LS Mean Diff. to Placebo [2]		-0.770		
LS SE Diff. to Placebo [2]		0.1698		
95% CI [2]		-1.107, -0.434		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.13 [-1.684, -0.569]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 13				
n (%)	34 (48.6)	34 (48.6)	23 (31.9)	22 (30.6)
Mean	2.3	-0.6	2.9	0.2
SD	1.24	1.12	0.88	0.66
Median	2.0	-0.3	3.0	0.0
Min, Max	1, 5	-4, 1	1, 4	-1, 2
LS Mean [2]		-0.696		0.278
LS SE [2]		0.1217		0.1371
95% CI [2]		-0.937, -0.455		0.007, 0.550
LS Mean Diff. to Placebo [2]		-0.974		
LS SE Diff. to Placebo [2]		0.1753		
95% CI [2]		-1.322, -0.627		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.42 [-2.021, -0.826]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	2.2	-0.7	3.1	0.1
SD	1.15	1.21	1.31	0.60
Median	2.0	-0.3	3.2	0.0
Min, Max	1, 5	-4, 1	1, 5	-1, 1
LS Mean [2]		-0.673		0.150
LS SE [2]		0.1249		0.1416
95% CI [2]		-0.921, -0.426		-0.130, 0.430
LS Mean Diff. to Placebo [2]		-0.823		
LS SE Diff. to Placebo [2]		0.1811		
95% CI [2]		-1.182, -0.465		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.19 [-1.781, -0.599]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	2.3	-0.7	3.1	0.2
SD	1.25	1.18	1.24	0.83
Median	2.0	-0.7	3.0	0.0
Min, Max	1, 5	-4, 1	1, 5	-2, 1
LS Mean [2]		-0.649		0.156
LS SE [2]		0.1273		0.1420
95% CI [2]		-0.901, -0.397		-0.125, 0.436
LS Mean Diff. to Placebo [2]		-0.805		
LS SE Diff. to Placebo [2]		0.1828		
95% CI [2]		-1.167, -0.443		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.16 [-1.753, -0.574]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	21 (29.2)	21 (29.2)
Mean	2.2	-0.6	3.1	0.0
SD	1.15	1.04	1.24	0.81
Median	2.0	-0.3	3.3	0.0
Min, Max	1, 5	-4, 1	1, 5	-2, 2
LS Mean [2]		-0.602		0.212
LS SE [2]		0.1284		0.1479
95% CI [2]		-0.857, -0.348		-0.081, 0.505
LS Mean Diff. to Placebo [2]		-0.814		
LS SE Diff. to Placebo [2]		0.1891		
95% CI [2]		-1.189, -0.439		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.13 [-1.710, -0.543]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	2.2	-0.7	2.8	0.1
SD	1.22	1.09	1.48	0.83
Median	2.0	-0.3	3.0	0.0
Min, Max	1, 5	-4, 1	1, 5	-2, 1
LS Mean [2]		-0.655		0.161
LS SE [2]		0.1260		0.1471
95% CI [2]		-0.904, -0.405		-0.130, 0.452
LS Mean Diff. to Placebo [2]		-0.816		
LS SE Diff. to Placebo [2]		0.1865		
95% CI [2]		-1.185, -0.446		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.19 [-1.799, -0.574]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	20 (27.8)
Mean	2.2	-0.7	3.0	0.2
SD	1.18	1.06	1.19	0.81
Median	2.0	-0.3	3.0	0.2
Min, Max	1, 5	-4, 1	1, 5	-1, 2
LS Mean [2]		-0.693		0.104
LS SE [2]		0.1303		0.1527
95% CI [2]		-0.951, -0.434		-0.199, 0.406
LS Mean Diff. to Placebo [2]		-0.797		
LS SE Diff. to Placebo [2]		0.1936		
95% CI [2]		-1.181, -0.413		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.10 [-1.692, -0.505]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	19 (26.4)
Mean	2.2	-0.5	2.7	0.1
SD	1.07	1.29	1.21	0.75
Median	2.0	-0.3	2.8	0.0
Min, Max	1, 5	-4, 1	1, 4	-1, 1
LS Mean [2]		-0.525		0.043
LS SE [2]		0.1294		0.1560
95% CI [2]		-0.782, -0.269		-0.265, 0.352
LS Mean Diff. to Placebo [2]		-0.569		
LS SE Diff. to Placebo [2]		0.1954		
95% CI [2]		-0.956, -0.181		
One-sided p-value [2]		0.0022		
Hedge's G (95% CI)		-0.78 [-1.361, -0.199]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	2.1	-0.8	3.1	0.2
SD	1.08	1.21	1.32	0.83
Median	1.8	-0.5	3.3	0.0
Min, Max	1, 4	-4, 1	1, 5	-2, 2
LS Mean [2]		-0.727		0.270
LS SE [2]		0.1320		0.1633
95% CI [2]		-0.988, -0.465		-0.054, 0.594
LS Mean Diff. to Placebo [2]		-0.997		
LS SE Diff. to Placebo [2]		0.2033		
95% CI [2]		-1.400, -0.593		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.40 [-2.070, -0.729]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	15 (20.8)	15 (20.8)
Mean	2.2	-0.8	3.1	0.1
SD	1.12	1.13	1.29	0.96
Median	2.0	-0.3	3.3	0.0
Min, Max	1, 4	-4, 2	1, 5	-2, 2
LS Mean [2]		-0.696		0.181
LS SE [2]		0.1233		0.1578
95% CI [2]		-0.940, -0.451		-0.132, 0.493
LS Mean Diff. to Placebo [2]		-0.876		
LS SE Diff. to Placebo [2]		0.1932		
95% CI [2]		-1.259, -0.493		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.28 [-1.949, -0.617]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	2.3	-0.7	3.1	0.1
SD	1.20	1.29	1.24	0.81
Median	2.0	-0.3	3.3	0.0
Min, Max	1, 5	-4, 2	1, 5	-2, 2
LS Mean [2]		-0.611		0.165
LS SE [2]		0.1330		0.1628
95% CI [2]		-0.874, -0.347		-0.158, 0.487
LS Mean Diff. to Placebo [2]		-0.775		
LS SE Diff. to Placebo [2]		0.2038		
95% CI [2]		-1.180, -0.371		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		-1.06 [-1.671, -0.455]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	14 (19.4)	14 (19.4)
Mean	2.4	-0.5	3.0	0.2
SD	1.33	1.09	1.09	0.93
Median	2.0	-0.3	3.3	0.2
Min, Max	1, 5	-4, 1	1, 4	-2, 2
LS Mean [2]		-0.645		0.268
LS SE [2]		0.1308		0.1697
95% CI [2]		-0.904, -0.385		-0.069, 0.605
LS Mean Diff. to Placebo [2]		-0.913		
LS SE Diff. to Placebo [2]		0.2082		
95% CI [2]		-1.327, -0.499		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.31 [-2.007, -0.616]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	1.9	-0.9	2.6	0.0
SD	1.14	1.27	1.13	0.84
Median	1.3	-0.3	2.3	0.0
Min, Max	1, 4	-4, 0	1, 4	-2, 1
LS Mean [2]		-0.760		0.155
LS SE [2]		0.1313		0.1721
95% CI [2]		-1.023, -0.497		-0.190, 0.499
LS Mean Diff. to Placebo [2]		-0.915		
LS SE Diff. to Placebo [2]		0.2109		
95% CI [2]		-1.337, -0.493		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.51 [-2.325, -0.690]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	1.5	-1.1	3.1	-0.1
SD	0.81	1.26	0.76	0.61
Median	1.0	-0.3	3.3	-0.3
Min, Max	1, 4	-4, 0	2, 4	-1, 1
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	1.8	-1.1	3.3	-0.1
SD	0.97	1.34	1.43	0.33
Median	1.3	-1.0	3.8	0.0
Min, Max	1, 4	-4, 1	1, 5	-1, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	1.8	-0.7	3.8	0.1
SD	1.18	1.11	1.45	0.57
Median	1.3	-0.7	4.2	0.2
Min, Max	1, 4	-3, 1	2, 5	-1, 1
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	2.4	-0.5	3.5	1.0
SD	1.27	1.07	1.65	0.00
Median	2.2	-0.3	3.5	1.0
Min, Max	1, 5	-3, 1	2, 5	1, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 29				
n (%)	12 (17.1)	12 (17.1)	3 (4.2)	3 (4.2)
Mean	2.3	-0.4	3.9	0.6
SD	1.10	0.90	1.39	0.51
Median	2.2	-0.3	4.3	0.7
Min, Max	1, 4	-2, 1	2, 5	0, 1
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	2.1	-0.6	3.5	-0.3
SD	1.22	0.61	1.69	1.10
Median	1.7	-0.3	3.8	-0.2
Min, Max	1, 4	-2, 0	1, 5	-2, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Sleep Score				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	5 (6.9)	5 (6.9)
Mean	2.5	-0.7	2.7	0.0
SD	1.15	0.97	1.04	1.13
Median	2.0	-0.3	2.7	0.0
Min, Max	1, 5	-2, 1	2, 4	-2, 1
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	2.4	-0.9	2.2	0.3
SD	1.18	1.03	0.24	0.94
Median	2.0	-1.0	2.2	0.3
Min, Max	1, 4	-2, 1	2, 2	0, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	2.1	-0.9		
SD	0.73	1.15		
Median	2.3	-0.7		
Min, Max	1, 3	-2, 1		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	1.0	-0.3		
SD	NA	NA		
Median	1.0	-0.3		
Min, Max	1, 1	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	1.0	-1.0		
SD	NA	NA		
Median	1.0	-1.0		
Min, Max	1, 1	-1, -1		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	1.0	-1.0		
SD	NA	NA		
Median	1.0	-1.0		
Min, Max	1, 1	-1, -1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Sleep Score				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	3.7	1.0		
SD	NA	NA		
Median	3.7	1.0		
Min, Max	4, 4	1, 1		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	3.0	-0.4	3.7	0.3
SD	0.80	1.08	NA	NA
Median	3.0	-0.3	3.7	0.3
Min, Max	2, 4	-2, 1	4, 4	0, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	4.6		4.7	
SD	2.72		2.91	
Median	4.8		4.6	
Min, Max	0, 10		0, 10	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Effect over Study Duration				
n (%)		68 (97.1)		68 (94.4)
LS Mean [2]		-1.726		-0.503
LS SE [2]		0.2116		0.2223
95% CI [2]		-2.144, -1.307		-0.942, -0.064
LS Mean Diff. to Placebo [2]		-1.222		
LS SE Diff. to Placebo [2]		0.2877		
95% CI [2]		-1.791, -0.654		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.68 [-1.029, -0.337]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 2				
n (%)	60 (85.7)	60 (85.7)	55 (76.4)	54 (75.0)
Mean	3.7	-1.1	3.7	-0.8
SD	2.45	2.02	2.68	1.85
Median	3.3	-0.8	2.8	-0.7
Min, Max	0, 10	-8, 3	0, 10	-9, 3
LS Mean [2]		-1.147		-0.880
LS SE [2]		0.2704		0.2754
95% CI [2]		-1.683, -0.612		-1.426, -0.335
LS Mean Diff. to Placebo [2]		-0.267		
LS SE Diff. to Placebo [2]		0.3711		
95% CI [2]		-1.002, 0.469		
One-sided p-value [2]		0.2368		
Hedge's G (95% CI)		-0.13 [-0.498, 0.239]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	60 (83.3)	60 (83.3)
Mean	3.1	-1.5	3.9	-0.8
SD	2.61	1.88	2.77	1.69
Median	2.0	-1.3	3.5	-0.5
Min, Max	0, 10	-6, 2	0, 10	-4, 3
LS Mean [2]		-1.539		-0.898
LS SE [2]		0.2714		0.2631
95% CI [2]		-2.076, -1.002		-1.419, -0.377
LS Mean Diff. to Placebo [2]		-0.641		
LS SE Diff. to Placebo [2]		0.3626		
95% CI [2]		-1.360, 0.077		
One-sided p-value [2]		0.0399		
Hedge's G (95% CI)		-0.32 [-0.691, 0.053]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	37 (51.4)	36 (50.0)
Mean	2.8	-1.4	4.5	-0.2
SD	2.23	1.88	2.81	1.80
Median	2.1	-1.2	4.3	-0.3
Min, Max	0, 10	-6, 2	0, 10	-4, 4
LS Mean [2]		-1.426		-0.321
LS SE [2]		0.2973		0.3106
95% CI [2]		-2.016, -0.835		-0.938, 0.296
LS Mean Diff. to Placebo [2]		-1.104		
LS SE Diff. to Placebo [2]		0.4166		
95% CI [2]		-1.932, -0.277		
One-sided p-value [2]		0.0048		
Hedge's G (95% CI)		-0.57 [-1.011, -0.121]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 5				
n (%)	43 (61.4)	43 (61.4)	42 (58.3)	42 (58.3)
Mean	2.9	-1.9	4.5	-0.2
SD	2.36	2.22	3.03	2.53
Median	2.7	-1.7	4.1	-0.3
Min, Max	0, 9	-8, 3	0, 10	-5, 6
LS Mean [2]		-1.621		-0.392
LS SE [2]		0.3552		0.3572
95% CI [2]		-2.326, -0.917		-1.100, 0.317
LS Mean Diff. to Placebo [2]		-1.230		
LS SE Diff. to Placebo [2]		0.4913		
95% CI [2]		-2.205, -0.254		
One-sided p-value [2]		0.0070		
Hedge's G (95% CI)		-0.53 [-0.962, -0.097]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	3.2	-1.1	3.7	-0.8
SD	2.50	2.36	2.69	2.14
Median	2.7	-0.9	3.3	-0.8
Min, Max	0, 9	-7, 6	0, 10	-5, 4
LS Mean [2]		-1.412		-0.971
LS SE [2]		0.2995		0.3058
95% CI [2]		-2.005, -0.818		-1.577, -0.365
LS Mean Diff. to Placebo [2]		-0.440		
LS SE Diff. to Placebo [2]		0.4144		
95% CI [2]		-1.262, 0.382		
One-sided p-value [2]		0.1452		
Hedge's G (95% CI)		-0.24 [-0.702, 0.220]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	37 (51.4)	36 (50.0)
Mean	2.9	-1.5	4.5	-0.6
SD	2.53	2.23	2.87	2.38
Median	1.8	-1.0	4.3	-0.5
Min, Max	0, 10	-6, 2	0, 10	-6, 4
LS Mean [2]		-1.580		-0.492
LS SE [2]		0.2879		0.3007
95% CI [2]		-2.149, -1.010		-1.087, 0.104
LS Mean Diff. to Placebo [2]		-1.088		
LS SE Diff. to Placebo [2]		0.4030		
95% CI [2]		-1.886, -0.290		
One-sided p-value [2]		0.0040		
Hedge's G (95% CI)		-0.59 [-1.040, -0.136]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	31 (43.1)	30 (41.7)
Mean	3.1	-1.6	4.7	0.0
SD	2.77	2.16	2.89	2.31
Median	2.2	-1.5	4.7	0.4
Min, Max	0, 10	-7, 3	0, 10	-5, 4
LS Mean [2]		-1.749		-0.412
LS SE [2]		0.2935		0.3195
95% CI [2]		-2.330, -1.167		-1.045, 0.221
LS Mean Diff. to Placebo [2]		-1.337		
LS SE Diff. to Placebo [2]		0.4203		
95% CI [2]		-2.170, -0.504		
One-sided p-value [2]		0.0010		
Hedge's G (95% CI)		-0.72 [-1.201, -0.240]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	34 (47.2)
Mean	2.8	-1.9	4.3	-0.1
SD	2.61	2.40	2.71	2.16
Median	1.7	-1.7	3.5	-0.1
Min, Max	0, 10	-9, 3	0, 10	-5, 6
LS Mean [2]		-1.603		-0.446
LS SE [2]		0.2879		0.3067
95% CI [2]		-2.174, -1.033		-1.053, 0.161
LS Mean Diff. to Placebo [2]		-1.158		
LS SE Diff. to Placebo [2]		0.4060		
95% CI [2]		-1.962, -0.353		
One-sided p-value [2]		0.0026		
Hedge's G (95% CI)		-0.62 [-1.081, -0.165]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 10				
n (%)	39 (55.7)	39 (55.7)	28 (38.9)	28 (38.9)
Mean	2.6	-1.7	4.9	0.5
SD	2.45	2.76	2.71	1.86
Median	2.0	-1.7	4.5	0.1
Min, Max	0, 9	-9, 5	0, 10	-3, 8
LS Mean [2]		-1.565		-0.210
LS SE [2]		0.3117		0.3404
95% CI [2]		-2.183, -0.947		-0.884, 0.465
LS Mean Diff. to Placebo [2]		-1.355		
LS SE Diff. to Placebo [2]		0.4479		
95% CI [2]		-2.243, -0.466		
One-sided p-value [2]		0.0016		
Hedge's G (95% CI)		-0.72 [-1.218, -0.217]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	2.9	-1.4	4.7	0.2
SD	2.50	2.98	2.94	1.75
Median	1.8	-1.7	4.2	0.2
Min, Max	0, 8	-8, 4	0, 10	-4, 4
LS Mean [2]		-1.640		-0.435
LS SE [2]		0.3496		0.3790
95% CI [2]		-2.334, -0.947		-1.187, 0.316
LS Mean Diff. to Placebo [2]		-1.205		
LS SE Diff. to Placebo [2]		0.5032		
95% CI [2]		-2.204, -0.206		
One-sided p-value [2]		0.0093		
Hedge's G (95% CI)		-0.60 [-1.126, -0.083]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 12				
n (%)	35 (50.0)	35 (50.0)	24 (33.3)	24 (33.3)
Mean	3.1	-1.7	4.0	-0.1
SD	2.41	2.86	2.50	1.54
Median	2.5	-1.3	3.5	0.0
Min, Max	0, 8	-9, 5	0, 9	-3, 2
LS Mean [2]		-1.528		-0.566
LS SE [2]		0.2932		0.3302
95% CI [2]		-2.109, -0.947		-1.220, 0.088
LS Mean Diff. to Placebo [2]		-0.962		
LS SE Diff. to Placebo [2]		0.4284		
95% CI [2]		-1.811, -0.112		
One-sided p-value [2]		0.0134		
Hedge's G (95% CI)		-0.57 [-1.099, -0.040]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 13				
n (%)	34 (48.6)	34 (48.6)	23 (31.9)	22 (30.6)
Mean	3.2	-1.3	4.1	-0.6
SD	2.78	2.36	2.46	1.90
Median	2.1	-1.0	4.0	-0.5
Min, Max	0, 10	-7, 3	0, 9	-5, 3
LS Mean [2]		-1.452		-0.729
LS SE [2]		0.2729		0.3138
95% CI [2]		-1.993, -0.911		-1.351, -0.108
LS Mean Diff. to Placebo [2]		-0.723		
LS SE Diff. to Placebo [2]		0.4015		
95% CI [2]		-1.519, 0.074		
One-sided p-value [2]		0.0374		
Hedge's G (95% CI)		-0.47 [-1.011, 0.076]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	22 (30.6)	21 (29.2)
Mean	2.4	-2.1	4.6	-0.4
SD	2.67	2.63	2.63	1.47
Median	1.5	-2.0	4.7	-0.3
Min, Max	0, 9	-9, 3	1, 9	-4, 2
LS Mean [2]		-1.939		-0.619
LS SE [2]		0.3059		0.3546
95% CI [2]		-2.546, -1.332		-1.322, 0.085
LS Mean Diff. to Placebo [2]		-1.321		
LS SE Diff. to Placebo [2]		0.4558		
95% CI [2]		-2.226, -0.416		
One-sided p-value [2]		0.0023		
Hedge's G (95% CI)		-0.77 [-1.340, -0.207]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	2.6	-2.2	5.2	-0.3
SD	2.25	2.24	2.89	1.93
Median	1.8	-1.8	5.0	-0.2
Min, Max	0, 9	-8, 1	0, 10	-4, 3
LS Mean [2]		-2.070		-0.218
LS SE [2]		0.2735		0.3131
95% CI [2]		-2.612, -1.527		-0.839, 0.402
LS Mean Diff. to Placebo [2]		-1.851		
LS SE Diff. to Placebo [2]		0.4005		
95% CI [2]		-2.646, -1.057		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.23 [-1.828, -0.639]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 16				
n (%)	34 (48.6)	34 (48.6)	21 (29.2)	21 (29.2)
Mean	3.0	-1.7	5.3	-0.1
SD	2.89	2.79	2.66	2.05
Median	2.3	-1.5	5.0	0.0
Min, Max	0, 10	-8, 5	0, 10	-5, 3
LS Mean [2]		-1.600		-0.130
LS SE [2]		0.3082		0.3633
95% CI [2]		-2.211, -0.990		-0.850, 0.589
LS Mean Diff. to Placebo [2]		-1.470		
LS SE Diff. to Placebo [2]		0.4640		
95% CI [2]		-2.390, -0.551		
One-sided p-value [2]		0.0010		
Hedge's G (95% CI)		-0.84 [-1.407, -0.275]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	2.4	-2.1	4.4	-0.4
SD	2.20	2.31	2.84	1.55
Median	1.8	-1.8	3.5	0.3
Min, Max	0, 9	-8, 1	0, 9	-4, 2
LS Mean [2]		-2.188		-0.526
LS SE [2]		0.2569		0.3030
95% CI [2]		-2.697, -1.678		-1.127, 0.074
LS Mean Diff. to Placebo [2]		-1.662		
LS SE Diff. to Placebo [2]		0.3841		
95% CI [2]		-2.424, -0.900		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.18 [-1.794, -0.569]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	20 (27.8)
Mean	2.7	-1.7	4.7	0.3
SD	2.66	2.76	2.75	2.06
Median	2.0	-1.3	4.7	-0.1
Min, Max	0, 9	-8, 3	0, 10	-4, 4
LS Mean [2]		-1.875		-0.211
LS SE [2]		0.3162		0.3763
95% CI [2]		-2.502, -1.248		-0.957, 0.534
LS Mean Diff. to Placebo [2]		-1.663		
LS SE Diff. to Placebo [2]		0.4792		
95% CI [2]		-2.614, -0.713		
One-sided p-value [2]		0.0004		
Hedge's G (95% CI)		-0.94 [-1.524, -0.357]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	20 (27.8)	19 (26.4)
Mean	3.1	-1.7	4.3	-0.1
SD	2.79	2.33	2.73	2.44
Median	3.0	-1.3	3.9	-0.3
Min, Max	0, 10	-8, 2	0, 9	-4, 6
LS Mean [2]		-1.622		-0.382
LS SE [2]		0.3045		0.3747
95% CI [2]		-2.226, -1.017		-1.126, 0.361
LS Mean Diff. to Placebo [2]		-1.239		
LS SE Diff. to Placebo [2]		0.4708		
95% CI [2]		-2.174, -0.304		
One-sided p-value [2]		0.0050		
Hedge's G (95% CI)		-0.72 [-1.296, -0.140]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	2.7	-2.0	4.6	-0.4
SD	2.33	2.49	2.77	2.23
Median	2.9	-1.8	3.8	-0.4
Min, Max	0, 9	-8, 2	0, 9	-6, 3
LS Mean [2]		-1.905		-0.441
LS SE [2]		0.3236		0.4098
95% CI [2]		-2.548, -1.261		-1.256, 0.374
LS Mean Diff. to Placebo [2]		-1.464		
LS SE Diff. to Placebo [2]		0.5111		
95% CI [2]		-2.481, -0.447		
One-sided p-value [2]		0.0027		
Hedge's G (95% CI)		-0.83 [-1.463, -0.202]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	15 (20.8)	15 (20.8)
Mean	2.5	-2.3	4.1	-0.4
SD	2.45	2.72	2.44	2.38
Median	2.2	-1.8	3.8	-0.7
Min, Max	0, 9	-8, 3	0, 8	-6, 5
LS Mean [2]		-2.066		-0.644
LS SE [2]		0.3295		0.4313
95% CI [2]		-2.722, -1.411		-1.501, 0.213
LS Mean Diff. to Placebo [2]		-1.423		
LS SE Diff. to Placebo [2]		0.5328		
95% CI [2]		-2.483, -0.363		
One-sided p-value [2]		0.0046		
Hedge's G (95% CI)		-0.77 [-1.408, -0.142]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	2.5	-2.2	4.2	-0.5
SD	2.20	2.28	2.50	1.79
Median	2.0	-1.8	3.3	-0.7
Min, Max	0, 9	-8, 2	0, 9	-5, 4
LS Mean [2]		-1.982		-0.538
LS SE [2]		0.2524		0.3116
95% CI [2]		-2.483, -1.480		-1.156, 0.081
LS Mean Diff. to Placebo [2]		-1.444		
LS SE Diff. to Placebo [2]		0.3879		
95% CI [2]		-2.215, -0.673		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-1.04 [-1.647, -0.434]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	13 (18.1)	13 (18.1)
Mean	2.8	-2.0	5.2	0.0
SD	2.75	2.53	2.45	1.89
Median	2.5	-2.2	4.0	-0.7
Min, Max	0, 10	-8, 2	2, 9	-2, 5
LS Mean [2]		-2.107		-0.237
LS SE [2]		0.2789		0.3752
95% CI [2]		-2.661, -1.553		-0.982, 0.508
LS Mean Diff. to Placebo [2]		-1.870		
LS SE Diff. to Placebo [2]		0.4555		
95% CI [2]		-2.775, -0.965		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.26 [-1.965, -0.550]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	2.1	-2.8	4.0	-0.2
SD	2.54	2.66	2.61	1.62
Median	1.2	-2.7	3.7	-0.8
Min, Max	0, 8	-9, 2	0, 8	-2, 3
LS Mean [2]		-2.072		-0.871
LS SE [2]		0.3255		0.4296
95% CI [2]		-2.722, -1.422		-1.730, -0.013
LS Mean Diff. to Placebo [2]		-1.201		
LS SE Diff. to Placebo [2]		0.5307		
95% CI [2]		-2.262, -0.139		
One-sided p-value [2]		0.0136		
Hedge's G (95% CI)		-0.80 [-1.552, -0.041]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	1.7	-2.7	5.9	0.5
SD	1.40	2.35	2.34	2.31
Median	1.7	-2.5	5.3	0.2
Min, Max	0, 4	-8, 1	3, 9	-2, 4
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	2.2	-2.2	5.3	1.6
SD	1.88	1.72	2.36	2.36
Median	2.2	-2.2	4.2	1.3
Min, Max	0, 6	-6, 1	3, 9	-2, 6

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	1.9	-3.1	4.1	-0.1
SD	2.02	2.50	2.57	1.06
Median	1.3	-3.1	3.3	-0.3
Min, Max	0, 7	-8, 1	2, 8	-1, 1
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	1.9	-2.8	6.4	0.3
SD	1.33	2.03	2.47	2.00
Median	1.9	-3.1	6.4	0.3
Min, Max	0, 4	-6, 1	5, 8	-1, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 29				
n (%)	12 (17.1)	12 (17.1)	3 (4.2)	3 (4.2)
Mean	2.1	-2.3	4.9	-0.8
SD	1.34	2.21	2.87	2.12
Median	2.1	-2.2	4.0	-1.8
Min, Max	0, 5	-5, 1	3, 8	-2, 2
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	1.8	-3.2	5.5	-1.4
SD	1.00	2.19	3.50	4.76
Median	1.6	-3.7	4.8	-0.7
Min, Max	1, 3	-6, 1	2, 10	-8, 4

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	1.6	-2.8	6.0	0.8
SD	0.84	2.60	2.51	0.99
Median	2.0	-4.0	6.3	0.4
Min, Max	0, 3	-6, 0	3, 9	0, 2
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	1.6	-2.7	2.5	-1.7
SD	0.66	2.46	1.41	0.94
Median	1.7	-2.8	2.5	-1.7
Min, Max	1, 3	-5, 0	2, 4	-2, -1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	2.3	-2.7		
SD	2.40	2.26		
Median	1.7	-3.3		
Min, Max	0, 6	-5, 0		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	1.3	-3.0		
SD	NA	NA		
Median	1.3	-3.0		
Min, Max	1, 1	-3, -3		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Emotion Score				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-8.5		
SD	NA	NA		
Median	0.0	-8.5		
Min, Max	0, 0	-9, -9		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-8.5		
SD	NA	NA		
Median	0.0	-8.5		
Min, Max	0, 0	-9, -9		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.2.1
Summary and Change from Baseline in DTIS Scores by Visit - Double-Blind Phase
Physical Functioning Score, Sleep Score, Emotion Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Emotion Score				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	2.0	-1.7		
SD	NA	NA		
Median	2.0	-1.7		
Min, Max	2, 2	-2, -2		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	4.4	-0.2	9.0	-0.7
SD	2.94	1.91	NA	NA
Median	4.7	0.0	9.0	-0.7
Min, Max	0, 9	-4, 3	9, 9	-1, -1

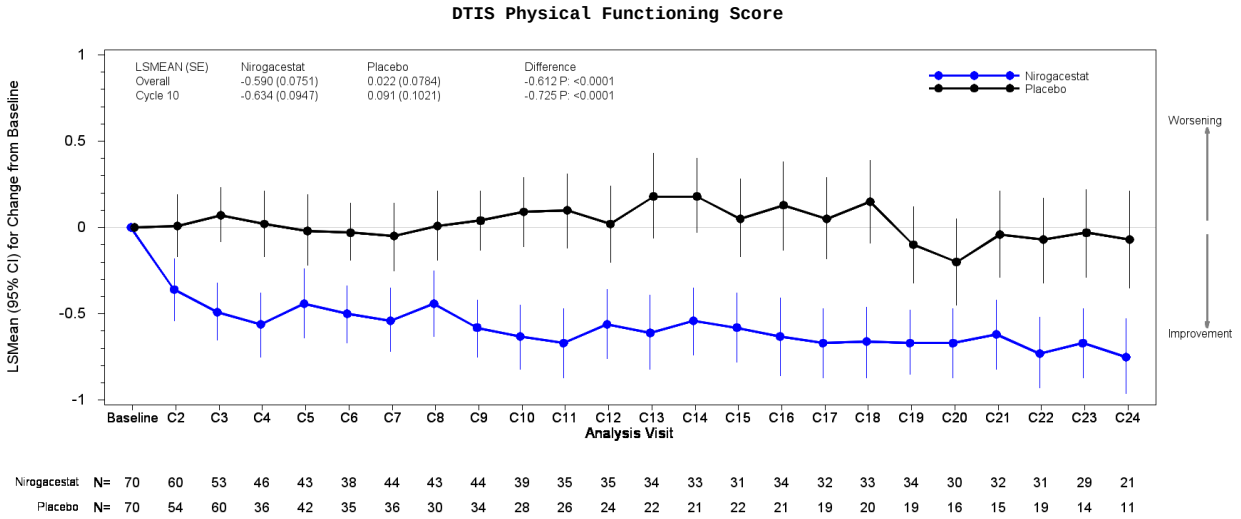
Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTIS = Desmoid Tumor Impact Scale; LS = Least squares; SE= Standard error
Note: A positive change from Baseline value indicated worsening impact and a negative change from Baseline value indicated improvement in impact. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

1.3.2 Figure MMRM DTIS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.2.2
Mixed Model Repeated Measures: Change from Baseline in DTIS Scores by Visit - Double Blind Phase
Intent-to-Treat Population

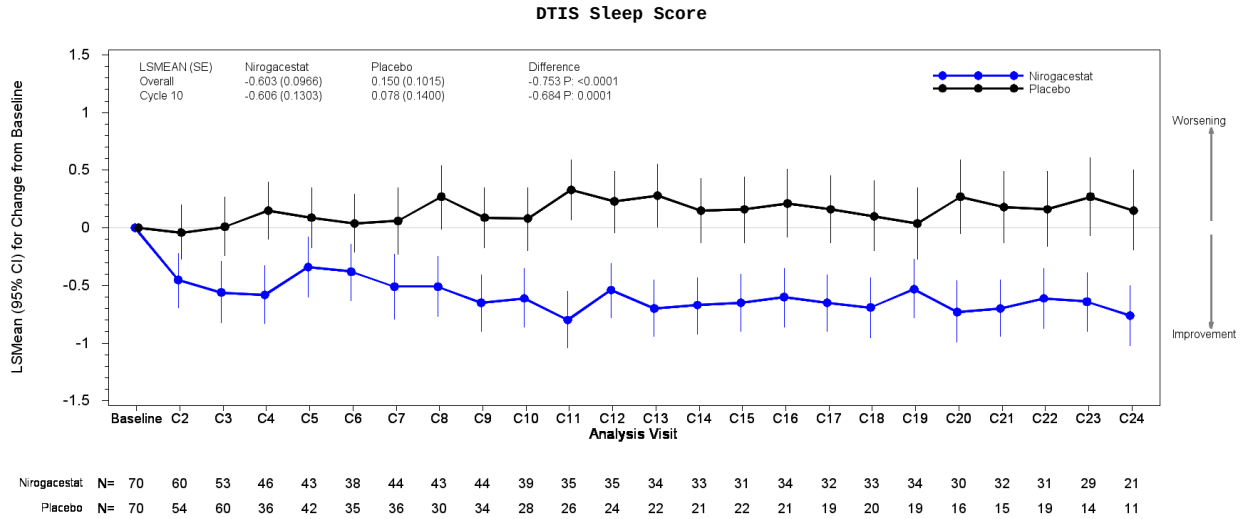


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.2.1, Dataset(s): ADSL, ADQS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.2.2
Mixed Model Repeated Measures: Change from Baseline in DTIS Scores by Visit - Double Blind Phase
Intent-to-Treat Population

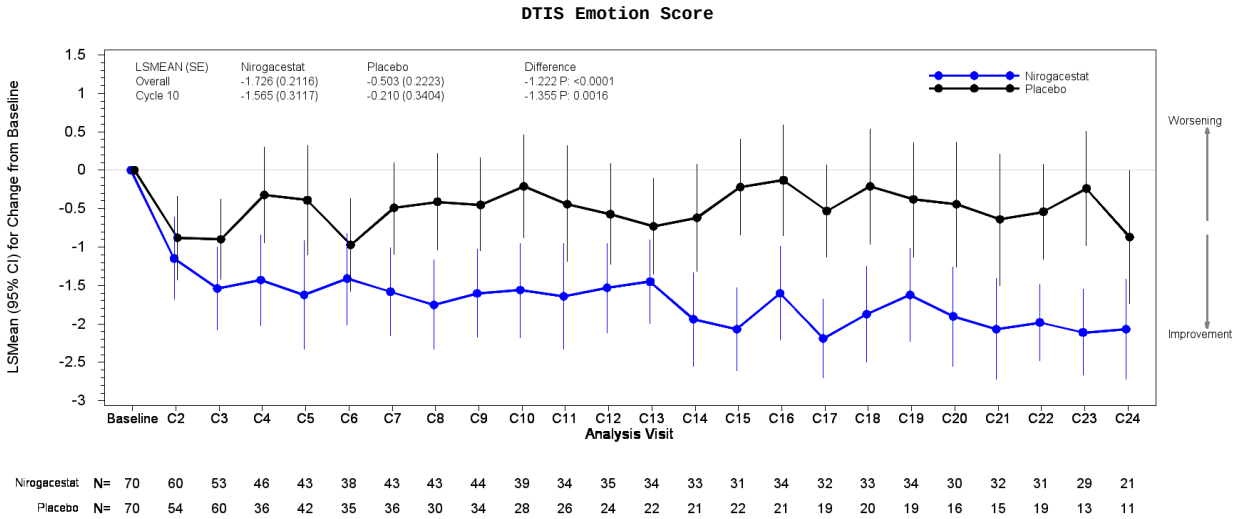


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.2.1, Dataset(s): ADSL, ADQS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.2.2
Mixed Model Repeated Measures: Change from Baseline in DTIS Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.2.1, Dataset(s): ADSL, ADQS

1.4 GODDESS DTSS

1.4.1 Table MMRM DTSS

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	3.3		3.5	
SD	2.33		2.57	
Median	3.2		3.2	
Min, Max	0, 8		0, 9	
Effect over Study Duration				
n (%)		67 (95.7)		69 (95.8)
LS Mean [2]		-1.232		0.191
LS SE [2]		0.1760		0.1790
95% CI [2]		-1.580, -0.885		-0.162, 0.545
LS Mean Diff. to Placebo [2]		-1.424		
LS SE Diff. to Placebo [2]		0.2358		
95% CI [2]		-1.890, -0.958		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.97 [-1.328, -0.617]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	61 (84.7)	61 (84.7)
Mean	2.4	-0.9	3.4	-0.1
SD	2.08	1.52	2.49	0.98
Median	1.9	-0.6	2.7	0.0
Min, Max	0, 8	-6, 2	0, 8	-3, 2
LS Mean [2]		-0.975		-0.121
LS SE [2]		0.2002		0.1977
95% CI [2]		-1.371, -0.579		-0.512, 0.270
LS Mean Diff. to Placebo [2]		-0.854		
LS SE Diff. to Placebo [2]		0.2678		
95% CI [2]		-1.384, -0.324		
One-sided p-value [2]		0.0009		
Hedge's G (95% CI)		-0.55 [-0.911, -0.188]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 3				
n (%)	57 (81.4)	57 (81.4)	62 (86.1)	62 (86.1)
Mean	2.4	-1.0	3.5	0.1
SD	2.17	1.48	2.55	1.21
Median	1.7	-0.8	3.0	0.0
Min, Max	0, 9	-5, 2	0, 9	-3, 3
LS Mean [2]		-1.097		0.106
LS SE [2]		0.2198		0.2156
95% CI [2]		-1.531, -0.662		-0.321, 0.532
LS Mean Diff. to Placebo [2]		-1.203		
LS SE Diff. to Placebo [2]		0.2957		
95% CI [2]		-1.788, -0.617		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.72 [-1.087, -0.345]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 4				
n (%)	44 (62.9)	44 (62.9)	43 (59.7)	43 (59.7)
Mean	1.8	-1.4	3.6	0.3
SD	1.79	1.85	2.70	1.09
Median	1.2	-1.1	3.5	0.1
Min, Max	0, 8	-7, 1	0, 10	-2, 4
LS Mean [2]		-1.161		0.276
LS SE [2]		0.2486		0.2452
95% CI [2]		-1.653, -0.669		-0.209, 0.761
LS Mean Diff. to Placebo [2]		-1.437		
LS SE Diff. to Placebo [2]		0.3381		
95% CI [2]		-2.107, -0.767		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.88 [-1.322, -0.442]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 5				
n (%)	45 (64.3)	45 (64.3)	46 (63.9)	45 (62.5)
Mean	1.8	-1.4	3.3	-0.1
SD	1.77	1.68	2.57	1.53
Median	1.4	-0.9	2.8	0.0
Min, Max	0, 7	-6, 2	0, 10	-5, 3
LS Mean [2]		-1.174		0.104
LS SE [2]		0.2375		0.2340
95% CI [2]		-1.644, -0.704		-0.359, 0.566
LS Mean Diff. to Placebo [2]		-1.278		
LS SE Diff. to Placebo [2]		0.3221		
95% CI [2]		-1.915, -0.640		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.81 [-1.238, -0.378]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 6				
n (%)	47 (67.1)	47 (67.1)	46 (63.9)	46 (63.9)
Mean	2.0	-1.2	3.3	0.0
SD	2.00	1.67	2.56	1.48
Median	1.5	-0.9	2.8	0.0
Min, Max	0, 9	-5, 3	0, 10	-4, 5
LS Mean [2]		-1.099		0.089
LS SE [2]		0.2232		0.2205
95% CI [2]		-1.541, -0.658		-0.347, 0.525
LS Mean Diff. to Placebo [2]		-1.189		
LS SE Diff. to Placebo [2]		0.3016		
95% CI [2]		-1.785, -0.592		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.79 [-1.207, -0.364]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 7				
n (%)	45 (64.3)	45 (64.3)	40 (55.6)	40 (55.6)
Mean	2.1	-1.0	3.5	0.0
SD	1.94	1.54	2.84	1.43
Median	1.6	-0.8	2.7	0.1
Min, Max	0, 8	-4, 2	0, 10	-3, 4
LS Mean [2]		-1.020		0.156
LS SE [2]		0.2207		0.2197
95% CI [2]		-1.457, -0.584		-0.279, 0.590
LS Mean Diff. to Placebo [2]		-1.176		
LS SE Diff. to Placebo [2]		0.2994		
95% CI [2]		-1.768, -0.583		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.82 [-1.261, -0.374]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 8				
n (%)	40 (57.1)	40 (57.1)	35 (48.6)	35 (48.6)
Mean	2.2	-1.4	3.7	0.2
SD	2.14	1.70	2.61	1.61
Median	1.8	-1.4	3.4	0.2
Min, Max	0, 8	-5, 2	0, 10	-3, 4
LS Mean [2]		-1.156		0.210
LS SE [2]		0.2113		0.2111
95% CI [2]		-1.574, -0.739		-0.207, 0.627
LS Mean Diff. to Placebo [2]		-1.366		
LS SE Diff. to Placebo [2]		0.2862		
95% CI [2]		-1.933, -0.800		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.05 [-1.538, -0.570]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 9				
n (%)	41 (58.6)	41 (58.6)	31 (43.1)	31 (43.1)
Mean	2.0	-1.5	4.1	0.2
SD	1.99	1.66	2.71	1.53
Median	1.5	-1.2	3.2	0.3
Min, Max	0, 8	-6, 1	0, 10	-4, 3
LS Mean [2]		-1.227		0.416
LS SE [2]		0.2077		0.2111
95% CI [2]		-1.638, -0.816		-0.001, 0.833
LS Mean Diff. to Placebo [2]		-1.643		
LS SE Diff. to Placebo [2]		0.2834		
95% CI [2]		-2.203, -1.082		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.30 [-1.810, -0.785]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 10				
n (%)	40 (57.1)	40 (57.1)	32 (44.4)	32 (44.4)
Mean	1.8	-1.5	4.1	0.4
SD	1.86	1.55	2.70	1.90
Median	1.3	-1.5	3.6	0.2
Min, Max	0, 7	-6, 1	0, 10	-4, 5
LS Mean [2]		-1.199		0.392
LS SE [2]		0.2122		0.2160
95% CI [2]		-1.619, -0.780		-0.035, 0.819
LS Mean Diff. to Placebo [2]		-1.591		
LS SE Diff. to Placebo [2]		0.2903		
95% CI [2]		-2.165, -1.017		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.23 [-1.740, -0.727]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 11				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	1.9	-1.4	3.6	0.1
SD	1.78	1.60	2.40	1.42
Median	1.4	-1.1	2.9	0.1
Min, Max	0, 7	-5, 1	0, 10	-2, 4
LS Mean [2]		-1.287		0.243
LS SE [2]		0.1881		0.1941
95% CI [2]		-1.659, -0.915		-0.140, 0.627
LS Mean Diff. to Placebo [2]		-1.530		
LS SE Diff. to Placebo [2]		0.2560		
95% CI [2]		-2.037, -1.024		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.38 [-1.927, -0.842]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 12				
n (%)	40 (57.1)	40 (57.1)	26 (36.1)	26 (36.1)
Mean	1.9	-1.4	3.4	-0.3
SD	1.71	1.53	2.39	1.72
Median	1.5	-1.2	3.0	-0.3
Min, Max	0, 7	-5, 1	0, 10	-4, 5
LS Mean [2]		-1.256		0.240
LS SE [2]		0.1908		0.2005
95% CI [2]		-1.633, -0.879		-0.156, 0.636
LS Mean Diff. to Placebo [2]		-1.496		
LS SE Diff. to Placebo [2]		0.2629		
95% CI [2]		-2.016, -0.976		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.31 [-1.857, -0.772]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	2.0	-1.6	3.7	0.0
SD	1.82	1.59	2.48	1.71
Median	1.6	-1.5	3.2	-0.4
Min, Max	0, 7	-5, 1	0, 9	-4, 4
LS Mean [2]		-1.232		0.289
LS SE [2]		0.1943		0.2059
95% CI [2]		-1.616, -0.848		-0.118, 0.695
LS Mean Diff. to Placebo [2]		-1.521		
LS SE Diff. to Placebo [2]		0.2695		
95% CI [2]		-2.054, -0.988		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.40 [-1.982, -0.813]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 14				
n (%)	35 (50.0)	35 (50.0)	25 (34.7)	25 (34.7)
Mean	1.9	-1.5	3.7	0.1
SD	1.87	1.63	2.74	1.74
Median	1.4	-1.1	3.0	0.0
Min, Max	0, 7	-6, 1	0, 10	-3, 4
LS Mean [2]		-1.303		0.306
LS SE [2]		0.1994		0.2105
95% CI [2]		-1.697, -0.909		-0.110, 0.721
LS Mean Diff. to Placebo [2]		-1.609		
LS SE Diff. to Placebo [2]		0.2767		
95% CI [2]		-2.156, -1.062		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.43 [-1.999, -0.852]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 15				
n (%)	39 (55.7)	39 (55.7)	23 (31.9)	23 (31.9)
Mean	2.0	-1.5	3.8	-0.2
SD	1.85	1.45	2.80	1.91
Median	1.8	-1.4	3.2	0.0
Min, Max	0, 7	-4, 1	0, 10	-4, 4
LS Mean [2]		-1.275		0.214
LS SE [2]		0.1857		0.1995
95% CI [2]		-1.642, -0.909		-0.180, 0.607
LS Mean Diff. to Placebo [2]		-1.489		
LS SE Diff. to Placebo [2]		0.2583		
95% CI [2]		-1.999, -0.979		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.37 [-1.935, -0.798]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 16				
n (%)	38 (54.3)	38 (54.3)	25 (34.7)	25 (34.7)
Mean	1.8	-1.6	3.5	-0.2
SD	1.77	1.54	2.68	2.07
Median	1.4	-1.5	3.2	0.0
Min, Max	0, 7	-5, 2	0, 10	-5, 3
LS Mean [2]		-1.336		0.061
LS SE [2]		0.1939		0.2079
95% CI [2]		-1.719, -0.953		-0.349, 0.471
LS Mean Diff. to Placebo [2]		-1.397		
LS SE Diff. to Placebo [2]		0.2707		
95% CI [2]		-1.932, -0.862		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.23 [-1.778, -0.681]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 17				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	1.8	-1.6	3.8	0.6
SD	1.73	1.21	2.73	1.51
Median	1.6	-1.6	3.1	0.5
Min, Max	0, 7	-4, 1	0, 10	-3, 4
LS Mean [2]		-1.444		0.267
LS SE [2]		0.1829		0.1985
95% CI [2]		-1.805, -1.082		-0.125, 0.659
LS Mean Diff. to Placebo [2]		-1.711		
LS SE Diff. to Placebo [2]		0.2558		
95% CI [2]		-2.216, -1.205		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.68 [-2.304, -1.063]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	21 (29.2)
Mean	1.8	-1.6	3.7	0.3
SD	1.57	1.60	2.85	1.98
Median	1.6	-1.2	3.5	0.0
Min, Max	0, 6	-5, 2	0, 10	-3, 4
LS Mean [2]		-1.346		0.269
LS SE [2]		0.2036		0.2230
95% CI [2]		-1.749, -0.944		-0.171, 0.709
LS Mean Diff. to Placebo [2]		-1.615		
LS SE Diff. to Placebo [2]		0.2890		
95% CI [2]		-2.186, -1.044		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.45 [-2.060, -0.837]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	23 (31.9)	23 (31.9)
Mean	1.8	-1.4	2.9	-0.1
SD	1.56	1.41	2.07	1.92
Median	1.5	-1.0	2.8	0.1
Min, Max	0, 5	-4, 1	0, 8	-4, 3
LS Mean [2]		-1.246		0.080
LS SE [2]		0.1928		0.2130
95% CI [2]		-1.627, -0.865		-0.341, 0.500
LS Mean Diff. to Placebo [2]		-1.326		
LS SE Diff. to Placebo [2]		0.2736		
95% CI [2]		-1.867, -0.785		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.22 [-1.798, -0.648]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 20				
n (%)	33 (47.1)	33 (47.1)	17 (23.6)	17 (23.6)
Mean	1.9	-1.4	3.1	-0.4
SD	1.69	1.86	2.29	1.99
Median	1.9	-1.3	3.1	-0.2
Min, Max	0, 6	-6, 4	0, 7	-3, 3
LS Mean [2]		-1.098		0.256
LS SE [2]		0.2256		0.2591
95% CI [2]		-1.544, -0.652		-0.256, 0.767
LS Mean Diff. to Placebo [2]		-1.353		
LS SE Diff. to Placebo [2]		0.3329		
95% CI [2]		-2.012, -0.695		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.10 [-1.729, -0.481]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 21				
n (%)	35 (50.0)	35 (50.0)	14 (19.4)	14 (19.4)
Mean	1.9	-1.5	3.5	0.0
SD	1.83	1.28	2.35	2.09
Median	1.7	-1.3	3.3	0.0
Min, Max	0, 7	-4, 1	0, 7	-3, 3
LS Mean [2]		-1.312		0.132
LS SE [2]		0.1888		0.2221
95% CI [2]		-1.685, -0.939		-0.306, 0.571
LS Mean Diff. to Placebo [2]		-1.444		
LS SE Diff. to Placebo [2]		0.2788		
95% CI [2]		-1.995, -0.893		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.36 [-2.034, -0.683]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 22				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	1.5	-1.5	3.2	-0.3
SD	1.44	1.35	2.20	1.96
Median	1.5	-1.6	2.9	-0.4
Min, Max	0, 6	-4, 2	0, 7	-3, 3
LS Mean [2]		-1.374		0.101
LS SE [2]		0.1892		0.2171
95% CI [2]		-1.748, -1.000		-0.328, 0.530
LS Mean Diff. to Placebo [2]		-1.475		
LS SE Diff. to Placebo [2]		0.2750		
95% CI [2]		-2.019, -0.931		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.44 [-2.069, -0.804]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 23				
n (%)	30 (42.9)	30 (42.9)	15 (20.8)	15 (20.8)
Mean	1.9	-1.3	2.8	0.2
SD	1.80	1.48	2.17	1.78
Median	1.8	-1.2	2.9	0.0
Min, Max	0, 8	-4, 2	0, 7	-3, 3
LS Mean [2]		-1.351		0.161
LS SE [2]		0.2020		0.2392
95% CI [2]		-1.751, -0.951		-0.312, 0.634
LS Mean Diff. to Placebo [2]		-1.512		
LS SE Diff. to Placebo [2]		0.3004		
95% CI [2]		-2.106, -0.918		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.41 [-2.098, -0.728]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 24				
n (%)	23 (32.9)	23 (32.9)	12 (16.7)	12 (16.7)
Mean	1.9	-1.3	3.3	0.1
SD	1.87	1.25	2.48	1.76
Median	1.4	-1.1	2.8	0.1
Min, Max	0, 7	-3, 2	0, 7	-3, 3
LS Mean [2]		-1.377		0.152
LS SE [2]		0.1871		0.2220
95% CI [2]		-1.747, -1.006		-0.288, 0.591
LS Mean Diff. to Placebo [2]		-1.528		
LS SE Diff. to Placebo [2]		0.2779		
95% CI [2]		-2.079, -0.978		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.74 [-2.552, -0.935]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score				
Cycle 25				
n (%)	21 (30.0)	21 (30.0)	6 (8.3)	6 (8.3)
Mean	1.7	-1.3	4.9	0.0
SD	1.87	1.42	2.95	1.71
Median	1.2	-1.3	5.4	-0.5
Min, Max	0, 7	-4, 2	1, 8	-2, 2
Cycle 26				
n (%)	13 (18.6)	13 (18.6)	4 (5.6)	4 (5.6)
Mean	2.0	-1.2	6.4	0.3
SD	2.06	1.49	2.47	1.21
Median	1.2	-1.0	7.5	0.4
Min, Max	0, 7	-4, 2	3, 8	-1, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score				
Cycle 27				
n (%)	14 (20.0)	14 (20.0)	3 (4.2)	3 (4.2)
Mean	2.1	-1.2	5.8	0.2
SD	2.06	1.45	2.22	2.26
Median	1.8	-1.1	6.7	1.3
Min, Max	0, 7	-4, 2	3, 7	-2, 2
Cycle 28				
n (%)	16 (22.9)	16 (22.9)	3 (4.2)	3 (4.2)
Mean	2.2	-1.3	5.0	0.8
SD	1.84	1.48	1.69	2.69
Median	1.9	-0.9	4.7	1.6
Min, Max	0, 7	-4, 2	4, 7	-2, 3

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score				
Cycle 29				
n (%)	13 (18.6)	13 (18.6)	3 (4.2)	3 (4.2)
Mean	2.0	-1.5	4.9	0.5
SD	1.85	1.54	2.03	2.16
Median	1.3	-1.0	4.1	0.8
Min, Max	0, 6	-4, 1	3, 7	-2, 2
Cycle 30				
n (%)	12 (17.1)	12 (17.1)	5 (6.9)	5 (6.9)
Mean	1.6	-1.5	3.9	-0.8
SD	1.61	1.44	2.10	2.38
Median	1.3	-1.1	3.2	-1.8
Min, Max	0, 5	-4, 1	2, 7	-3, 3

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score				
Cycle 31				
n (%)	9 (12.9)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	1.9	-1.4	4.0	-1.1
SD	2.27	1.92	1.98	2.70
Median	1.4	-1.0	3.6	-2.0
Min, Max	0, 7	-4, 1	2, 7	-3, 3
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	1.9	-0.7	4.4	2.5
SD	2.28	1.31	1.27	1.48
Median	1.4	-0.5	4.4	2.5
Min, Max	0, 6	-3, 1	3, 5	2, 4

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score				
Cycle 33				
n (%)	6 (8.6)	6 (8.6)	0	0
Mean	2.3	-1.7		
SD	2.38	2.13		
Median	1.6	-1.9		
Min, Max	0, 7	-4, 1		
Cycle 34				
n (%)	4 (5.7)	4 (5.7)	0	0
Mean	1.9	-2.0		
SD	3.02	1.99		
Median	0.6	-1.8		
Min, Max	0, 6	-4, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.6		
SD	NA	NA		
Median	0.0	-2.6		
Min, Max	0, 0	-3, -3		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.6		
SD	NA	NA		
Median	0.0	-2.6		
Min, Max	0, 0	-3, -3		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	2.0	1.0		
SD	NA	NA		
Median	2.0	1.0		
Min, Max	2, 2	1, 1		
Follow-Up				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	2.4	-1.0		
SD	2.47	2.78		
Median	1.4	0.4		
Min, Max	0, 6	-6, 1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	3.4		3.6	
SD	2.36		2.58	
Median	3.3		3.3	
Min, Max	0, 9		0, 9	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Effect over Study Duration				
n (%)		67 (95.7)		69 (95.8)
LS Mean [2]		-1.253		0.174
LS SE [2]		0.1760		0.1792
95% CI [2]		-1.601, -0.905		-0.180, 0.528
LS Mean Diff. to Placebo [2]		-1.427		
LS SE Diff. to Placebo [2]		0.2363		
95% CI [2]		-1.894, -0.960		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.97 [-1.329, -0.618]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	61 (84.7)	61 (84.7)
Mean	2.4	-0.9	3.5	-0.1
SD	2.13	1.50	2.51	0.98
Median	2.0	-0.6	2.8	0.0
Min, Max	0, 8	-6, 2	0, 9	-3, 2
LS Mean [2]		-0.992		-0.123
LS SE [2]		0.2002		0.1978
95% CI [2]		-1.389, -0.596		-0.514, 0.269
LS Mean Diff. to Placebo [2]		-0.870		
LS SE Diff. to Placebo [2]		0.2681		
95% CI [2]		-1.400, -0.339		
One-sided p-value [2]		0.0008		
Hedge's G (95% CI)		-0.56 [-0.921, -0.198]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 3				
n (%)	57 (81.4)	57 (81.4)	62 (86.1)	62 (86.1)
Mean	2.5	-1.1	3.5	0.0
SD	2.21	1.47	2.56	1.23
Median	1.9	-0.8	3.2	0.0
Min, Max	0, 9	-5, 2	0, 9	-3, 3
LS Mean [2]		-1.108		0.093
LS SE [2]		0.2202		0.2160
95% CI [2]		-1.544, -0.673		-0.334, 0.520
LS Mean Diff. to Placebo [2]		-1.201		
LS SE Diff. to Placebo [2]		0.2965		
95% CI [2]		-1.788, -0.614		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.71 [-1.085, -0.343]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 4				
n (%)	44 (62.9)	44 (62.9)	43 (59.7)	43 (59.7)
Mean	1.9	-1.5	3.7	0.4
SD	1.83	1.86	2.72	1.11
Median	1.2	-1.3	3.5	0.1
Min, Max	0, 8	-7, 1	0, 10	-2, 4
LS Mean [2]		-1.175		0.267
LS SE [2]		0.2502		0.2469
95% CI [2]		-1.670, -0.680		-0.221, 0.756
LS Mean Diff. to Placebo [2]		-1.442		
LS SE Diff. to Placebo [2]		0.3407		
95% CI [2]		-2.117, -0.767		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.88 [-1.320, -0.440]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 5				
n (%)	45 (64.3)	45 (64.3)	46 (63.9)	45 (62.5)
Mean	1.9	-1.4	3.4	-0.1
SD	1.82	1.67	2.60	1.54
Median	1.4	-0.9	2.8	0.0
Min, Max	0, 7	-6, 2	0, 10	-5, 3
LS Mean [2]		-1.194		0.082
LS SE [2]		0.2353		0.2319
95% CI [2]		-1.660, -0.729		-0.377, 0.541
LS Mean Diff. to Placebo [2]		-1.276		
LS SE Diff. to Placebo [2]		0.3192		
95% CI [2]		-1.908, -0.644		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.81 [-1.244, -0.384]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 6				
n (%)	47 (67.1)	47 (67.1)	46 (63.9)	46 (63.9)
Mean	2.1	-1.3	3.3	0.0
SD	2.04	1.68	2.61	1.49
Median	1.5	-0.8	2.8	0.0
Min, Max	0, 9	-5, 3	0, 10	-3, 5
LS Mean [2]		-1.134		0.084
LS SE [2]		0.2229		0.2203
95% CI [2]		-1.574, -0.693		-0.352, 0.520
LS Mean Diff. to Placebo [2]		-1.218		
LS SE Diff. to Placebo [2]		0.3015		
95% CI [2]		-1.814, -0.621		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.81 [-1.228, -0.383]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 7				
n (%)	45 (64.3)	45 (64.3)	40 (55.6)	40 (55.6)
Mean	2.2	-1.1	3.6	0.0
SD	1.99	1.56	2.85	1.47
Median	1.6	-0.8	2.8	0.1
Min, Max	0, 8	-4, 2	0, 10	-3, 4
LS Mean [2]		-1.026		0.123
LS SE [2]		0.2204		0.2196
95% CI [2]		-1.462, -0.590		-0.312, 0.557
LS Mean Diff. to Placebo [2]		-1.148		
LS SE Diff. to Placebo [2]		0.2994		
95% CI [2]		-1.741, -0.556		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.80 [-1.242, -0.357]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 8				
n (%)	40 (57.1)	40 (57.1)	35 (48.6)	35 (48.6)
Mean	2.3	-1.5	3.7	0.1
SD	2.19	1.69	2.63	1.65
Median	1.8	-1.3	3.5	0.2
Min, Max	0, 8	-5, 2	0, 10	-3, 4
LS Mean [2]		-1.179		0.186
LS SE [2]		0.2119		0.2119
95% CI [2]		-1.598, -0.760		-0.233, 0.605
LS Mean Diff. to Placebo [2]		-1.365		
LS SE Diff. to Placebo [2]		0.2874		
95% CI [2]		-1.933, -0.796		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.05 [-1.533, -0.566]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 9				
n (%)	41 (58.6)	41 (58.6)	31 (43.1)	31 (43.1)
Mean	2.0	-1.6	4.2	0.2
SD	2.05	1.67	2.72	1.56
Median	1.5	-1.0	3.4	0.2
Min, Max	0, 8	-6, 1	0, 10	-4, 3
LS Mean [2]		-1.253		0.408
LS SE [2]		0.2077		0.2114
95% CI [2]		-1.664, -0.843		-0.010, 0.825
LS Mean Diff. to Placebo [2]		-1.661		
LS SE Diff. to Placebo [2]		0.2838		
95% CI [2]		-2.222, -1.100		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.31 [-1.825, -0.798]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 10				
n (%)	40 (57.1)	40 (57.1)	32 (44.4)	32 (44.4)
Mean	1.9	-1.5	4.2	0.4
SD	1.95	1.57	2.72	1.93
Median	1.3	-1.5	3.9	0.3
Min, Max	0, 8	-6, 1	0, 10	-4, 5
LS Mean [2]		-1.208		0.372
LS SE [2]		0.2143		0.2184
95% CI [2]		-1.631, -0.784		-0.060, 0.803
LS Mean Diff. to Placebo [2]		-1.579		
LS SE Diff. to Placebo [2]		0.2938		
95% CI [2]		-2.160, -0.998		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.21 [-1.717, -0.707]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 11				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	2.0	-1.4	3.7	0.1
SD	1.84	1.61	2.42	1.48
Median	1.5	-1.2	3.0	0.1
Min, Max	0, 7	-5, 1	0, 10	-3, 4
LS Mean [2]		-1.299		0.217
LS SE [2]		0.1894		0.1958
95% CI [2]		-1.673, -0.924		-0.170, 0.604
LS Mean Diff. to Placebo [2]		-1.516		
LS SE Diff. to Placebo [2]		0.2585		
95% CI [2]		-2.027, -1.004		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.36 [-1.901, -0.820]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 12				
n (%)	40 (57.1)	40 (57.1)	26 (36.1)	26 (36.1)
Mean	1.9	-1.5	3.5	-0.3
SD	1.77	1.54	2.40	1.75
Median	1.5	-1.3	3.0	-0.3
Min, Max	0, 7	-5, 1	0, 10	-3, 5
LS Mean [2]		-1.268		0.217
LS SE [2]		0.1920		0.2022
95% CI [2]		-1.648, -0.889		-0.182, 0.617
LS Mean Diff. to Placebo [2]		-1.485		
LS SE Diff. to Placebo [2]		0.2653		
95% CI [2]		-2.010, -0.961		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.30 [-1.837, -0.755]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	2.1	-1.6	3.7	0.0
SD	1.87	1.61	2.48	1.71
Median	1.6	-1.6	3.2	-0.4
Min, Max	0, 7	-5, 2	0, 9	-3, 4
LS Mean [2]		-1.256		0.264
LS SE [2]		0.1951		0.2072
95% CI [2]		-1.642, -0.871		-0.145, 0.674
LS Mean Diff. to Placebo [2]		-1.521		
LS SE Diff. to Placebo [2]		0.2714		
95% CI [2]		-2.057, -0.984		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.39 [-1.974, -0.806]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 14				
n (%)	35 (50.0)	35 (50.0)	25 (34.7)	25 (34.7)
Mean	1.9	-1.5	3.8	0.1
SD	1.95	1.66	2.78	1.82
Median	1.4	-1.0	3.1	0.0
Min, Max	0, 7	-6, 1	0, 10	-3, 4
LS Mean [2]		-1.313		0.293
LS SE [2]		0.2032		0.2147
95% CI [2]		-1.714, -0.912		-0.131, 0.717
LS Mean Diff. to Placebo [2]		-1.606		
LS SE Diff. to Placebo [2]		0.2829		
95% CI [2]		-2.165, -1.047		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.40 [-1.966, -0.825]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 15				
n (%)	39 (55.7)	39 (55.7)	23 (31.9)	23 (31.9)
Mean	2.1	-1.6	3.9	-0.2
SD	1.91	1.46	2.84	1.96
Median	1.9	-1.3	3.2	0.0
Min, Max	0, 7	-4, 1	0, 10	-4, 4
LS Mean [2]		-1.296		0.212
LS SE [2]		0.1878		0.2022
95% CI [2]		-1.666, -0.925		-0.187, 0.611
LS Mean Diff. to Placebo [2]		-1.508		
LS SE Diff. to Placebo [2]		0.2621		
95% CI [2]		-2.026, -0.990		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.37 [-1.936, -0.799]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 16				
n (%)	38 (54.3)	38 (54.3)	25 (34.7)	25 (34.7)
Mean	1.9	-1.6	3.6	-0.2
SD	1.83	1.54	2.71	2.12
Median	1.4	-1.5	3.2	0.0
Min, Max	0, 7	-5, 2	0, 10	-5, 3
LS Mean [2]		-1.353		0.029
LS SE [2]		0.1960		0.2107
95% CI [2]		-1.740, -0.966		-0.386, 0.445
LS Mean Diff. to Placebo [2]		-1.382		
LS SE Diff. to Placebo [2]		0.2746		
95% CI [2]		-1.925, -0.840		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.20 [-1.749, -0.655]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 17				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	1.9	-1.6	3.8	0.6
SD	1.79	1.19	2.74	1.57
Median	1.6	-1.6	3.1	0.6
Min, Max	0, 7	-4, 1	0, 10	-3, 4
LS Mean [2]		-1.480		0.257
LS SE [2]		0.1848		0.2011
95% CI [2]		-1.845, -1.115		-0.140, 0.654
LS Mean Diff. to Placebo [2]		-1.737		
LS SE Diff. to Placebo [2]		0.2594		
95% CI [2]		-2.250, -1.225		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.69 [-2.312, -1.070]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	21 (29.2)
Mean	1.8	-1.6	3.7	0.3
SD	1.65	1.59	2.87	2.03
Median	1.6	-1.3	3.4	0.1
Min, Max	0, 6	-5, 1	0, 10	-3, 4
LS Mean [2]		-1.368		0.259
LS SE [2]		0.2061		0.2263
95% CI [2]		-1.775, -0.960		-0.187, 0.706
LS Mean Diff. to Placebo [2]		-1.627		
LS SE Diff. to Placebo [2]		0.2936		
95% CI [2]		-2.207, -1.047		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.44 [-2.051, -0.829]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	23 (31.9)	23 (31.9)
Mean	1.9	-1.4	2.9	-0.1
SD	1.64	1.43	2.05	1.95
Median	1.6	-1.0	2.8	0.2
Min, Max	0, 6	-4, 2	0, 8	-4, 3
LS Mean [2]		-1.252		0.058
LS SE [2]		0.1958		0.2167
95% CI [2]		-1.639, -0.865		-0.370, 0.486
LS Mean Diff. to Placebo [2]		-1.310		
LS SE Diff. to Placebo [2]		0.2788		
95% CI [2]		-1.861, -0.759		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.19 [-1.761, -0.617]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 20				
n (%)	33 (47.1)	33 (47.1)	17 (23.6)	17 (23.6)
Mean	2.0	-1.4	3.1	-0.5
SD	1.76	1.86	2.30	2.01
Median	1.9	-1.3	3.1	-0.2
Min, Max	0, 7	-6, 4	0, 7	-4, 3
LS Mean [2]		-1.108		0.223
LS SE [2]		0.2280		0.2625
95% CI [2]		-1.559, -0.657		-0.296, 0.741
LS Mean Diff. to Placebo [2]		-1.331		
LS SE Diff. to Placebo [2]		0.3374		
95% CI [2]		-1.998, -0.663		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.07 [-1.696, -0.453]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 21				
n (%)	35 (50.0)	35 (50.0)	14 (19.4)	14 (19.4)
Mean	1.9	-1.5	3.5	0.0
SD	1.88	1.30	2.34	2.05
Median	1.8	-1.4	3.3	0.0
Min, Max	0, 7	-4, 2	0, 7	-3, 3
LS Mean [2]		-1.344		0.105
LS SE [2]		0.1881		0.2220
95% CI [2]		-1.716, -0.972		-0.334, 0.543
LS Mean Diff. to Placebo [2]		-1.449		
LS SE Diff. to Placebo [2]		0.2785		
95% CI [2]		-1.999, -0.898		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.37 [-2.043, -0.691]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 22				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	1.6	-1.5	3.3	-0.3
SD	1.51	1.37	2.20	1.99
Median	1.5	-1.5	3.0	-0.4
Min, Max	0, 6	-4, 2	0, 7	-3, 3
LS Mean [2]		-1.404		0.088
LS SE [2]		0.1908		0.2193
95% CI [2]		-1.782, -1.027		-0.346, 0.521
LS Mean Diff. to Placebo [2]		-1.492		
LS SE Diff. to Placebo [2]		0.2781		
95% CI [2]		-2.042, -0.942		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.44 [-2.073, -0.808]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 23				
n (%)	30 (42.9)	30 (42.9)	15 (20.8)	15 (20.8)
Mean	1.9	-1.3	2.8	0.1
SD	1.85	1.48	2.13	1.79
Median	1.9	-1.2	3.1	0.0
Min, Max	0, 8	-4, 2	0, 7	-3, 3
LS Mean [2]		-1.394		0.157
LS SE [2]		0.2025		0.2403
95% CI [2]		-1.794, -0.993		-0.318, 0.632
LS Mean Diff. to Placebo [2]		-1.551		
LS SE Diff. to Placebo [2]		0.3017		
95% CI [2]		-2.147, -0.954		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.44 [-2.133, -0.757]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 24				
n (%)	23 (32.9)	23 (32.9)	12 (16.7)	12 (16.7)
Mean	1.9	-1.3	3.3	0.1
SD	1.92	1.28	2.52	1.74
Median	1.5	-1.1	2.8	0.1
Min, Max	0, 7	-3, 2	0, 7	-2, 3
LS Mean [2]		-1.417		0.128
LS SE [2]		0.1878		0.2232
95% CI [2]		-1.789, -1.045		-0.314, 0.570
LS Mean Diff. to Placebo [2]		-1.545		
LS SE Diff. to Placebo [2]		0.2796		
95% CI [2]		-2.099, -0.991		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.75 [-2.565, -0.945]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 25				
n (%)	21 (30.0)	21 (30.0)	6 (8.3)	6 (8.3)
Mean	1.7	-1.4	5.0	0.0
SD	1.90	1.46	2.99	1.72
Median	1.2	-1.2	5.5	-0.4
Min, Max	0, 7	-4, 2	1, 8	-2, 2
Cycle 26				
n (%)	13 (18.6)	13 (18.6)	4 (5.6)	4 (5.6)
Mean	2.0	-1.2	6.5	0.4
SD	2.11	1.54	2.53	1.17
Median	1.3	-1.0	7.6	0.4
Min, Max	0, 7	-3, 2	3, 8	-1, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 27				
n (%)	14 (20.0)	14 (20.0)	3 (4.2)	3 (4.2)
Mean	2.1	-1.3	5.9	0.3
SD	2.11	1.50	2.14	2.16
Median	1.8	-1.1	6.8	1.3
Min, Max	0, 7	-4, 2	4, 7	-2, 2
Cycle 28				
n (%)	16 (22.9)	16 (22.9)	3 (4.2)	3 (4.2)
Mean	2.2	-1.3	5.2	0.8
SD	1.86	1.49	1.77	2.46
Median	2.0	-1.0	4.7	1.5
Min, Max	0, 7	-4, 2	4, 7	-2, 3

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 29				
n (%)	13 (18.6)	13 (18.6)	3 (4.2)	3 (4.2)
Mean	2.0	-1.5	4.9	0.5
SD	1.89	1.56	2.09	2.07
Median	1.4	-1.0	4.2	0.9
Min, Max	0, 6	-4, 1	3, 7	-2, 2
Cycle 30				
n (%)	12 (17.1)	12 (17.1)	5 (6.9)	5 (6.9)
Mean	1.7	-1.5	4.0	-0.7
SD	1.64	1.46	2.11	2.29
Median	1.4	-1.2	3.2	-1.6
Min, Max	0, 5	-4, 1	2, 7	-3, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 31				
n (%)	9 (12.9)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	2.0	-1.5	4.1	-1.1
SD	2.28	1.91	1.99	2.63
Median	1.4	-1.0	3.6	-2.0
Min, Max	0, 7	-4, 1	2, 7	-3, 3
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	2.0	-0.7	4.4	2.5
SD	2.29	1.37	1.12	1.40
Median	1.5	-0.5	4.4	2.5
Min, Max	0, 6	-3, 1	4, 5	1, 3

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 33				
n (%)	6 (8.6)	6 (8.6)	0	0
Mean	2.3	-1.7		
SD	2.39	2.13		
Median	1.7	-2.0		
Min, Max	0, 7	-4, 1		
Cycle 34				
n (%)	4 (5.7)	4 (5.7)	0	0
Mean	1.9	-2.1		
SD	3.07	1.93		
Median	0.6	-1.9		
Min, Max	0, 6	-4, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.8		
SD	NA	NA		
Median	0.0	-2.8		
Min, Max	0, 0	-3, -3		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.9		
SD	NA	NA		
Median	0.0	-2.9		
Min, Max	0, 0	-3, -3		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptoms Score - 5 Items				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	2.3	1.0		
SD	NA	NA		
Median	2.3	1.0		
Min, Max	2, 2	1, 1		
Follow-Up				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	2.6	-0.9		
SD	2.57	2.77		
Median	1.5	0.4		
Min, Max	0, 6	-6, 1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Domain				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	3.6		3.9	
SD	2.57		2.80	
Median	3.3		3.5	
Min, Max	0, 9		0, 9	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Domain				
Effect over Study Duration				
n (%)		67 (95.7)		69 (95.8)
LS Mean [2]		-1.890		0.064
LS SE [2]		0.2248		0.2271
95% CI [2]		-2.334, -1.445		-0.384, 0.513
LS Mean Diff. to Placebo [2]		-1.954		
LS SE Diff. to Placebo [2]		0.2998		
95% CI [2]		-2.547, -1.361		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.05 [-1.407, -0.690]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	61 (84.7)	61 (84.7)
Mean	2.1	-1.5	3.6	-0.3
SD	2.26	1.82	2.69	1.48
Median	1.7	-1.0	3.3	0.0
Min, Max	0, 8	-7, 2	0, 8	-4, 3
LS Mean [2]		-1.550		-0.222
LS SE [2]		0.2520		0.2492
95% CI [2]		-2.048, -1.051		-0.715, 0.271
LS Mean Diff. to Placebo [2]		-1.327		
LS SE Diff. to Placebo [2]		0.3370		
95% CI [2]		-1.995, -0.660		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.68 [-1.043, -0.313]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 3				
n (%)	57 (81.4)	57 (81.4)	62 (86.1)	62 (86.1)
Mean	1.9	-1.9	3.5	-0.2
SD	2.33	2.23	2.70	1.77
Median	0.8	-1.6	3.2	-0.1
Min, Max	0, 9	-7, 2	0, 8	-5, 5
LS Mean [2]		-1.832		-0.029
LS SE [2]		0.2915		0.2857
95% CI [2]		-2.409, -1.255		-0.594, 0.536
LS Mean Diff. to Placebo [2]		-1.803		
LS SE Diff. to Placebo [2]		0.3932		
95% CI [2]		-2.582, -1.024		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.81 [-1.184, -0.436]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 4				
n (%)	44 (62.9)	44 (62.9)	43 (59.7)	43 (59.7)
Mean	1.4	-2.1	3.8	0.1
SD	1.89	2.59	2.86	1.45
Median	0.8	-1.5	3.2	0.1
Min, Max	0, 8	-8, 2	0, 10	-4, 3
LS Mean [2]		-1.918		0.141
LS SE [2]		0.3037		0.2996
95% CI [2]		-2.519, -1.317		-0.452, 0.734
LS Mean Diff. to Placebo [2]		-2.059		
LS SE Diff. to Placebo [2]		0.4121		
95% CI [2]		-2.875, -1.242		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.03 [-1.482, -0.587]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 5				
n (%)	45 (64.3)	45 (64.3)	46 (63.9)	45 (62.5)
Mean	1.6	-1.8	3.5	-0.4
SD	1.80	2.05	2.58	2.00
Median	1.0	-1.3	3.3	0.0
Min, Max	0, 7	-7, 4	0, 9	-6, 4
LS Mean [2]		-1.722		-0.022
LS SE [2]		0.2770		0.2721
95% CI [2]		-2.270, -1.174		-0.560, 0.517
LS Mean Diff. to Placebo [2]		-1.700		
LS SE Diff. to Placebo [2]		0.3726		
95% CI [2]		-2.438, -0.962		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.92 [-1.358, -0.488]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 6				
n (%)	47 (67.1)	47 (67.1)	46 (63.9)	46 (63.9)
Mean	1.6	-1.8	3.5	-0.2
SD	2.22	2.57	2.59	1.89
Median	0.7	-1.8	3.2	0.0
Min, Max	0, 10	-8, 6	0, 9	-5, 4
LS Mean [2]		-1.691		-0.014
LS SE [2]		0.2911		0.2875
95% CI [2]		-2.267, -1.115		-0.583, 0.555
LS Mean Diff. to Placebo [2]		-1.677		
LS SE Diff. to Placebo [2]		0.3942		
95% CI [2]		-2.457, -0.896		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.85 [-1.274, -0.425]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 7				
n (%)	45 (64.3)	45 (64.3)	40 (55.6)	40 (55.6)
Mean	1.7	-1.7	3.6	-0.5
SD	1.94	2.15	2.87	1.90
Median	1.1	-1.0	3.1	-0.1
Min, Max	0, 8	-7, 2	0, 10	-5, 2
LS Mean [2]		-1.580		-0.045
LS SE [2]		0.2821		0.2813
95% CI [2]		-2.138, -1.021		-0.601, 0.512
LS Mean Diff. to Placebo [2]		-1.535		
LS SE Diff. to Placebo [2]		0.3832		
95% CI [2]		-2.294, -0.776		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.83 [-1.278, -0.390]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 8				
n (%)	40 (57.1)	40 (57.1)	35 (48.6)	35 (48.6)
Mean	1.9	-2.0	3.7	-0.1
SD	2.23	2.20	2.71	2.03
Median	0.9	-1.6	3.4	0.0
Min, Max	0, 8	-8, 2	0, 10	-5, 5
LS Mean [2]		-1.624		0.185
LS SE [2]		0.2747		0.2752
95% CI [2]		-2.167, -1.080		-0.360, 0.729
LS Mean Diff. to Placebo [2]		-1.808		
LS SE Diff. to Placebo [2]		0.3731		
95% CI [2]		-2.547, -1.070		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.07 [-1.557, -0.587]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 9				
n (%)	41 (58.6)	41 (58.6)	31 (43.1)	31 (43.1)
Mean	1.6	-2.1	4.2	-0.2
SD	2.03	2.12	2.66	1.87
Median	1.0	-1.8	3.6	0.0
Min, Max	0, 7	-8, 1	0, 10	-5, 2
LS Mean [2]		-1.777		0.362
LS SE [2]		0.2649		0.2709
95% CI [2]		-2.301, -1.252		-0.174, 0.898
LS Mean Diff. to Placebo [2]		-2.139		
LS SE Diff. to Placebo [2]		0.3624		
95% CI [2]		-2.856, -1.421		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.32 [-1.836, -0.808]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 10				
n (%)	40 (57.1)	40 (57.1)	32 (44.4)	32 (44.4)
Mean	1.4	-2.2	4.1	0.1
SD	1.80	2.11	2.82	2.20
Median	0.8	-2.1	4.6	0.0
Min, Max	0, 7	-7, 1	0, 9	-6, 6
LS Mean [2]		-1.778		0.341
LS SE [2]		0.2746		0.2801
95% CI [2]		-2.321, -1.234		-0.213, 0.894
LS Mean Diff. to Placebo [2]		-2.118		
LS SE Diff. to Placebo [2]		0.3764		
95% CI [2]		-2.863, -1.373		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.27 [-1.776, -0.759]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 11				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	1.4	-2.0	3.4	-0.4
SD	1.84	2.13	2.22	1.52
Median	1.0	-1.5	3.2	-0.2
Min, Max	0, 7	-8, 1	0, 8	-4, 3
LS Mean [2]		-1.933		-0.034
LS SE [2]		0.2328		0.2408
95% CI [2]		-2.394, -1.472		-0.511, 0.442
LS Mean Diff. to Placebo [2]		-1.899		
LS SE Diff. to Placebo [2]		0.3157		
95% CI [2]		-2.524, -1.274		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.39 [-1.929, -0.844]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 12				
n (%)	40 (57.1)	40 (57.1)	26 (36.1)	26 (36.1)
Mean	1.5	-2.0	3.3	-0.8
SD	1.87	2.15	2.31	1.73
Median	1.1	-1.4	3.3	-0.9
Min, Max	0, 7	-7, 2	0, 9	-5, 3
LS Mean [2]		-1.754		0.144
LS SE [2]		0.2441		0.2580
95% CI [2]		-2.237, -1.271		-0.366, 0.654
LS Mean Diff. to Placebo [2]		-1.898		
LS SE Diff. to Placebo [2]		0.3374		
95% CI [2]		-2.566, -1.230		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.30 [-1.842, -0.760]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	1.4	-2.3	3.5	-0.4
SD	2.05	2.34	2.52	2.10
Median	0.8	-2.3	3.3	-0.4
Min, Max	0, 8	-8, 2	0, 9	-5, 5
LS Mean [2]		-1.819		0.314
LS SE [2]		0.2815		0.2990
95% CI [2]		-2.377, -1.262		-0.277, 0.906
LS Mean Diff. to Placebo [2]		-2.134		
LS SE Diff. to Placebo [2]		0.3958		
95% CI [2]		-2.917, -1.350		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.35 [-1.932, -0.771]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 14				
n (%)	35 (50.0)	35 (50.0)	25 (34.7)	25 (34.7)
Mean	1.3	-2.0	3.7	-0.2
SD	1.94	2.06	2.78	1.95
Median	0.2	-1.7	3.1	-0.1
Min, Max	0, 7	-7, 1	0, 8	-4, 5
LS Mean [2]		-1.914		0.145
LS SE [2]		0.2572		0.2718
95% CI [2]		-2.422, -1.405		-0.392, 0.682
LS Mean Diff. to Placebo [2]		-2.058		
LS SE Diff. to Placebo [2]		0.3576		
95% CI [2]		-2.766, -1.351		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.41 [-1.985, -0.841]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 15				
n (%)	39 (55.7)	39 (55.7)	23 (31.9)	23 (31.9)
Mean	1.4	-2.3	3.3	-1.0
SD	1.98	2.14	2.57	2.09
Median	0.7	-2.0	3.3	-0.3
Min, Max	0, 7	-8, 1	0, 9	-6, 2
LS Mean [2]		-1.979		-0.046
LS SE [2]		0.2450		0.2652
95% CI [2]		-2.463, -1.494		-0.570, 0.478
LS Mean Diff. to Placebo [2]		-1.932		
LS SE Diff. to Placebo [2]		0.3434		
95% CI [2]		-2.611, -1.253		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.34 [-1.908, -0.774]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 16				
n (%)	38 (54.3)	38 (54.3)	25 (34.7)	25 (34.7)
Mean	1.1	-2.4	3.6	-0.6
SD	1.76	2.18	2.85	2.62
Median	0.3	-2.2	3.7	0.0
Min, Max	0, 7	-8, 1	0, 9	-7, 5
LS Mean [2]		-2.090		-0.061
LS SE [2]		0.2559		0.2754
95% CI [2]		-2.595, -1.584		-0.604, 0.483
LS Mean Diff. to Placebo [2]		-2.029		
LS SE Diff. to Placebo [2]		0.3592		
95% CI [2]		-2.739, -1.319		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.35 [-1.908, -0.794]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 17				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	1.1	-2.3	3.8	0.2
SD	1.79	1.86	2.68	1.80
Median	0.6	-2.1	3.2	0.2
Min, Max	0, 7	-6, 1	0, 9	-5, 3
LS Mean [2]		-2.205		-0.024
LS SE [2]		0.2388		0.2591
95% CI [2]		-2.677, -1.732		-0.536, 0.488
LS Mean Diff. to Placebo [2]		-2.181		
LS SE Diff. to Placebo [2]		0.3343		
95% CI [2]		-2.842, -1.519		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.64 [-2.261, -1.027]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	21 (29.2)
Mean	1.0	-2.3	3.6	-0.3
SD	1.45	2.13	2.86	2.59
Median	0.5	-1.7	3.0	0.0
Min, Max	0, 5	-8, 1	0, 9	-6, 4
LS Mean [2]		-2.092		0.128
LS SE [2]		0.2549		0.2791
95% CI [2]		-2.597, -1.588		-0.423, 0.680
LS Mean Diff. to Placebo [2]		-2.221		
LS SE Diff. to Placebo [2]		0.3610		
95% CI [2]		-2.935, -1.507		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.59 [-2.215, -0.967]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	23 (31.9)	23 (31.9)
Mean	1.1	-2.1	2.9	-0.3
SD	1.49	2.10	2.24	2.53
Median	0.5	-1.5	3.1	-0.3
Min, Max	0, 5	-8, 1	0, 7	-6, 4
LS Mean [2]		-2.003		-0.150
LS SE [2]		0.2362		0.2591
95% CI [2]		-2.470, -1.536		-0.662, 0.362
LS Mean Diff. to Placebo [2]		-1.853		
LS SE Diff. to Placebo [2]		0.3319		
95% CI [2]		-2.509, -1.196		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.40 [-1.986, -0.810]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 20				
n (%)	33 (47.1)	33 (47.1)	17 (23.6)	17 (23.6)
Mean	1.3	-2.1	2.9	-0.8
SD	1.73	2.49	2.25	2.59
Median	0.7	-1.8	3.3	-0.8
Min, Max	0, 7	-8, 5	0, 7	-5, 5
LS Mean [2]		-1.840		0.194
LS SE [2]		0.2755		0.3169
95% CI [2]		-2.385, -1.295		-0.433, 0.820
LS Mean Diff. to Placebo [2]		-2.034		
LS SE Diff. to Placebo [2]		0.4056		
95% CI [2]		-2.837, -1.231		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.36 [-2.002, -0.716]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 21				
n (%)	35 (50.0)	35 (50.0)	14 (19.4)	14 (19.4)
Mean	1.1	-2.4	3.6	-0.3
SD	1.85	2.04	2.70	3.21
Median	0.5	-2.5	3.3	-0.7
Min, Max	0, 8	-7, 1	0, 9	-6, 6
LS Mean [2]		-2.113		-0.025
LS SE [2]		0.2452		0.2899
95% CI [2]		-2.598, -1.629		-0.597, 0.548
LS Mean Diff. to Placebo [2]		-2.089		
LS SE Diff. to Placebo [2]		0.3635		
95% CI [2]		-2.807, -1.370		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.51 [-2.200, -0.824]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 22				
n (%)	33 (47.1)	33 (47.1)	19 (26.4)	19 (26.4)
Mean	0.8	-2.4	3.2	-0.8
SD	1.24	2.06	2.35	2.75
Median	0.1	-2.5	2.8	-0.9
Min, Max	0, 6	-8, 1	0, 8	-5, 6
LS Mean [2]		-2.176		-0.245
LS SE [2]		0.2300		0.2613
95% CI [2]		-2.631, -1.722		-0.761, 0.272
LS Mean Diff. to Placebo [2]		-1.932		
LS SE Diff. to Placebo [2]		0.3304		
95% CI [2]		-2.585, -1.278		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.53 [-2.172, -0.898]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 23				
n (%)	30 (42.9)	30 (42.9)	15 (20.8)	15 (20.8)
Mean	1.2	-2.0	3.2	0.3
SD	1.86	1.93	2.52	2.55
Median	0.2	-1.6	2.9	0.0
Min, Max	0, 8	-6, 1	0, 8	-4, 6
LS Mean [2]		-2.018		0.200
LS SE [2]		0.2523		0.2957
95% CI [2]		-2.517, -1.519		-0.384, 0.785
LS Mean Diff. to Placebo [2]		-2.218		
LS SE Diff. to Placebo [2]		0.3709		
95% CI [2]		-2.952, -1.484		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.66 [-2.373, -0.955]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 24				
n (%)	23 (32.9)	23 (32.9)	12 (16.7)	12 (16.7)
Mean	1.1	-2.0	3.2	-0.3
SD	1.87	1.77	2.79	2.77
Median	0.0	-1.7	2.5	0.0
Min, Max	0, 7	-5, 1	0, 9	-5, 6
LS Mean [2]		-2.058		0.239
LS SE [2]		0.2514		0.2921
95% CI [2]		-2.557, -1.560		-0.340, 0.818
LS Mean Diff. to Placebo [2]		-2.298		
LS SE Diff. to Placebo [2]		0.3692		
95% CI [2]		-3.030, -1.566		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.96 [-2.797, -1.125]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 25				
n (%)	21 (30.0)	21 (30.0)	6 (8.3)	6 (8.3)
Mean	1.1	-1.7	4.2	-0.8
SD	1.92	1.57	2.66	1.87
Median	0.0	-1.6	4.3	-0.6
Min, Max	0, 7	-5, 1	1, 7	-3, 1
Cycle 26				
n (%)	13 (18.6)	13 (18.6)	4 (5.6)	4 (5.6)
Mean	1.5	-1.6	5.6	-0.7
SD	2.29	1.83	2.15	1.51
Median	0.3	-1.2	6.4	-0.4
Min, Max	0, 7	-5, 1	3, 7	-3, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Domain				
Cycle 27				
n (%)	14 (20.0)	14 (20.0)	3 (4.2)	3 (4.2)
Mean	1.5	-1.5	6.0	0.5
SD	2.18	1.69	1.13	4.68
Median	0.5	-1.2	6.6	1.3
Min, Max	0, 7	-5, 1	5, 7	-5, 5
Cycle 28				
n (%)	16 (22.9)	16 (22.9)	3 (4.2)	3 (4.2)
Mean	1.5	-1.5	4.6	0.5
SD	2.04	1.50	2.08	5.12
Median	0.7	-1.3	4.1	1.9
Min, Max	0, 7	-4, 1	3, 7	-5, 5

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Domain				
Cycle 29				
n (%)	13 (18.6)	13 (18.6)	3 (4.2)	3 (4.2)
Mean	1.3	-1.8	3.6	-0.9
SD	2.04	1.85	1.33	3.07
Median	0.0	-1.0	3.7	0.2
Min, Max	0, 6	-6, 0	2, 5	-4, 1
Cycle 30				
n (%)	12 (17.1)	12 (17.1)	5 (6.9)	5 (6.9)
Mean	1.0	-1.8	3.2	-2.0
SD	1.63	1.64	1.14	2.40
Median	0.0	-1.1	3.0	-3.3
Min, Max	0, 5	-5, 0	2, 5	-4, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Pain Domain				
Cycle 31				
n (%)	9 (12.9)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	1.1	-1.6	2.9	-2.6
SD	2.23	2.03	1.09	2.75
Median	0.3	-0.7	2.8	-3.4
Min, Max	0, 7	-5, 0	2, 4	-5, 1
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	1.4	-0.9	5.0	3.6
SD	2.51	1.56	2.93	2.09
Median	0.3	-0.5	5.0	3.6
Min, Max	0, 6	-4, 0	3, 7	2, 5

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 33				
n (%)	6 (8.6)	6 (8.6)	1 (1.4)	1 (1.4)
Mean	1.5	-2.2	6.8	4.8
SD	2.55	2.37	NA	NA
Median	0.4	-2.1	6.8	4.8
Min, Max	0, 7	-5, 0	7, 7	5, 5
Cycle 34				
n (%)	4 (5.7)	4 (5.7)	0	0
Mean	1.6	-1.5		
SD	3.23	1.42		
Median	0.0	-1.2		
Min, Max	0, 6	-3, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-1.8		
SD	NA	NA		
Median	0.0	-1.8		
Min, Max	0, 0	-2, -2		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-1.8		
SD	NA	NA		
Median	0.0	-1.8		
Min, Max	0, 0	-2, -2		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Pain Domain				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	2.9	1.3		
SD	NA	NA		
Median	2.9	1.3		
Min, Max	3, 3	1, 1		
Follow-Up				
n (%)	6 (8.6)	6 (8.6)	0	0
Mean	3.0	-0.9		
SD	2.54	2.58		
Median	2.4	-0.3		
Min, Max	1, 7	-6, 1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Baseline [1]				
n (%)	26 (37.1)		29 (40.3)	
Mean	1.3		2.2	
SD	1.61		2.15	
Median	0.7		1.7	
Min, Max	0, 6		0, 7	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Effect over Study Duration				
n (%)		24 (34.3)		29 (40.3)
LS Mean [2]		-0.204		-0.278
LS SE [2]		0.2368		0.2132
95% CI [2]		-0.680, 0.271		-0.705, 0.149
LS Mean Diff. to Placebo [2]		0.074		
LS SE Diff. to Placebo [2]		0.3178		
95% CI [2]		-0.564, 0.711		
One-sided p-value [2]		0.5912		
Hedge's G (95% CI)		0.06 [-0.477, 0.605]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 2				
n (%)	22 (31.4)	22 (31.4)	26 (36.1)	25 (34.7)
Mean	1.5	0.3	2.3	0.0
SD	1.25	0.94	2.24	1.09
Median	1.4	0.1	1.8	0.0
Min, Max	0, 5	-1, 2	0, 8	-3, 2
LS Mean [2]		0.262		0.103
LS SE [2]		0.2531		0.2218
95% CI [2]		-0.248, 0.772		-0.344, 0.550
LS Mean Diff. to Placebo [2]		0.159		
LS SE Diff. to Placebo [2]		0.3378		
95% CI [2]		-0.522, 0.839		
One-sided p-value [2]		0.6797		
Hedge's G (95% CI)		0.14 [-0.437, 0.710]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 3				
n (%)	22 (31.4)	22 (31.4)	27 (37.5)	27 (37.5)
Mean	1.5	0.3	1.9	-0.4
SD	1.11	0.99	2.19	1.50
Median	1.5	0.3	1.2	0.0
Min, Max	0, 4	-2, 2	0, 8	-6, 2
LS Mean [2]		0.143		-0.236
LS SE [2]		0.2747		0.2403
95% CI [2]		-0.408, 0.695		-0.719, 0.246
LS Mean Diff. to Placebo [2]		0.379		
LS SE Diff. to Placebo [2]		0.3667		
95% CI [2]		-0.357, 1.116		
One-sided p-value [2]		0.8472		
Hedge's G (95% CI)		0.29 [-0.271, 0.861]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 4				
n (%)	17 (24.3)	17 (24.3)	19 (26.4)	19 (26.4)
Mean	1.5	0.3	2.0	-0.2
SD	1.50	1.28	2.69	1.46
Median	1.1	0.5	1.1	0.0
Min, Max	0, 5	-3, 2	0, 9	-3, 2
LS Mean [2]		0.113		-0.295
LS SE [2]		0.3413		0.3045
95% CI [2]		-0.572, 0.799		-0.906, 0.317
LS Mean Diff. to Placebo [2]		0.408		
LS SE Diff. to Placebo [2]		0.4602		
95% CI [2]		-0.517, 1.333		
One-sided p-value [2]		0.8102		
Hedge's G (95% CI)		0.29 [-0.366, 0.950]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 5				
n (%)	15 (21.4)	15 (21.4)	23 (31.9)	22 (30.6)
Mean	1.2	0.0	1.9	-0.3
SD	1.37	1.08	2.20	1.79
Median	1.0	0.0	1.1	0.0
Min, Max	0, 5	-2, 2	0, 8	-6, 2
LS Mean [2]		0.062		-0.237
LS SE [2]		0.3062		0.2648
95% CI [2]		-0.552, 0.676		-0.769, 0.294
LS Mean Diff. to Placebo [2]		0.299		
LS SE Diff. to Placebo [2]		0.4059		
95% CI [2]		-0.515, 1.114		
One-sided p-value [2]		0.7680		
Hedge's G (95% CI)		0.24 [-0.418, 0.899]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 6				
n (%)	18 (25.7)	18 (25.7)	20 (27.8)	20 (27.8)
Mean	1.3	0.2	1.7	-0.4
SD	1.41	1.09	2.07	1.75
Median	1.1	0.1	1.3	0.0
Min, Max	0, 5	-2, 2	0, 8	-6, 2
LS Mean [2]		0.019		-0.306
LS SE [2]		0.2800		0.2497
95% CI [2]		-0.543, 0.581		-0.807, 0.195
LS Mean Diff. to Placebo [2]		0.325		
LS SE Diff. to Placebo [2]		0.3756		
95% CI [2]		-0.429, 1.079		
One-sided p-value [2]		0.8044		
Hedge's G (95% CI)		0.28 [-0.363, 0.916]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 7				
n (%)	17 (24.3)	17 (24.3)	17 (23.6)	17 (23.6)
Mean	1.5	0.2	1.6	-0.7
SD	1.54	1.37	2.35	1.89
Median	1.2	0.1	1.0	-0.1
Min, Max	0, 6	-2, 4	0, 9	-6, 3
LS Mean [2]		0.037		-0.472
LS SE [2]		0.3366		0.3063
95% CI [2]		-0.640, 0.715		-1.088, 0.144
LS Mean Diff. to Placebo [2]		0.509		
LS SE Diff. to Placebo [2]		0.4573		
95% CI [2]		-0.411, 1.429		
One-sided p-value [2]		0.8645		
Hedge's G (95% CI)		0.37 [-0.303, 1.053]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 8				
n (%)	13 (18.6)	13 (18.6)	17 (23.6)	17 (23.6)
Mean	0.9	-0.3	2.1	-0.5
SD	0.96	1.10	2.27	1.75
Median	0.5	-0.1	1.7	0.0
Min, Max	0, 3	-2, 1	0, 8	-6, 2
LS Mean [2]		-0.431		-0.229
LS SE [2]		0.2723		0.2405
95% CI [2]		-0.977, 0.115		-0.711, 0.254
LS Mean Diff. to Placebo [2]		-0.203		
LS SE Diff. to Placebo [2]		0.3647		
95% CI [2]		-0.934, 0.529		
One-sided p-value [2]		0.2905		
Hedge's G (95% CI)		-0.20 [-0.924, 0.524]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 9				
n (%)	14 (20.0)	14 (20.0)	14 (19.4)	14 (19.4)
Mean	0.9	-0.4	2.3	-0.5
SD	1.23	0.80	2.65	2.05
Median	0.5	-0.1	1.5	0.0
Min, Max	0, 4	-2, 1	0, 8	-6, 2
LS Mean [2]		-0.316		-0.313
LS SE [2]		0.2912		0.2691
95% CI [2]		-0.900, 0.268		-0.852, 0.226
LS Mean Diff. to Placebo [2]		-0.002		
LS SE Diff. to Placebo [2]		0.4000		
95% CI [2]		-0.804, 0.800		
One-sided p-value [2]		0.4977		
Hedge's G (95% CI)		-0.00 [-0.743, 0.739]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 10				
n (%)	14 (20.0)	14 (20.0)	15 (20.8)	15 (20.8)
Mean	0.9	-0.4	2.1	-0.7
SD	1.19	0.80	2.39	1.83
Median	0.4	-0.1	1.7	-0.3
Min, Max	0, 4	-2, 0	0, 8	-6, 2
LS Mean [2]		-0.368		-0.380
LS SE [2]		0.2510		0.2319
95% CI [2]		-0.872, 0.135		-0.844, 0.084
LS Mean Diff. to Placebo [2]		0.011		
LS SE Diff. to Placebo [2]		0.3442		
95% CI [2]		-0.678, 0.700		
One-sided p-value [2]		0.5129		
Hedge's G (95% CI)		0.01 [-0.717, 0.740]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 11				
n (%)	15 (21.4)	15 (21.4)	11 (15.3)	11 (15.3)
Mean	1.1	-0.5	2.1	-0.4
SD	1.79	0.83	1.84	0.67
Median	0.3	-0.3	1.8	-0.1
Min, Max	0, 6	-2, 0	0, 6	-1, 1
LS Mean [2]		-0.504		-0.274
LS SE [2]		0.2114		0.2060
95% CI [2]		-0.932, -0.076		-0.690, 0.142
LS Mean Diff. to Placebo [2]		-0.230		
LS SE Diff. to Placebo [2]		0.2951		
95% CI [2]		-0.826, 0.367		
One-sided p-value [2]		0.2203		
Hedge's G (95% CI)		-0.29 [-1.073, 0.491]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 12				
n (%)	16 (22.9)	16 (22.9)	10 (13.9)	10 (13.9)
Mean	1.6	-0.1	1.5	-1.1
SD	1.87	1.15	1.54	1.96
Median	0.9	0.0	1.5	-0.6
Min, Max	0, 6	-2, 2	0, 5	-6, 1
LS Mean [2]		-0.130		-0.344
LS SE [2]		0.3011		0.3082
95% CI [2]		-0.737, 0.477		-0.964, 0.275
LS Mean Diff. to Placebo [2]		0.214		
LS SE Diff. to Placebo [2]		0.4326		
95% CI [2]		-0.657, 1.085		
One-sided p-value [2]		0.6885		
Hedge's G (95% CI)		0.18 [-0.607, 0.976]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Cycle 13				
n (%)	15 (21.4)	15 (21.4)	9 (12.5)	9 (12.5)
Mean	1.6	0.0	1.4	-1.0
SD	2.31	1.28	1.95	2.13
Median	0.3	0.0	0.8	-0.2
Min, Max	0, 6	-2, 3	0, 6	-6, 1
Cycle 14				
n (%)	14 (20.0)	14 (20.0)	9 (12.5)	9 (12.5)
Mean	1.3	-0.2	2.0	-0.4
SD	1.97	0.77	1.52	1.11
Median	0.7	0.0	1.7	-0.6
Min, Max	0, 6	-2, 1	0, 5	-2, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 15				
n (%)	15 (21.4)	15 (21.4)	11 (15.3)	11 (15.3)
Mean	1.2	-0.4	2.4	-0.9
SD	1.83	0.78	2.36	1.73
Median	0.6	-0.1	1.7	-0.8
Min, Max	0, 6	-2, 1	0, 8	-5, 2
LS Mean [2]		-0.359		-0.385
LS SE [2]		0.2517		0.2575
95% CI [2]		-0.865, 0.147		-0.901, 0.131
LS Mean Diff. to Placebo [2]		0.026		
LS SE Diff. to Placebo [2]		0.3624		
95% CI [2]		-0.701, 0.753		
One-sided p-value [2]		0.5286		
Hedge's G (95% CI)		0.03 [-0.751, 0.805]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 16				
n (%)	15 (21.4)	15 (21.4)	13 (18.1)	13 (18.1)
Mean	1.0	-0.6	2.7	-0.5
SD	1.88	0.86	2.15	1.80
Median	0.1	-0.3	2.1	-0.1
Min, Max	0, 6	-2, 1	0, 7	-5, 2
LS Mean [2]		-0.598		-0.221
LS SE [2]		0.2503		0.2514
95% CI [2]		-1.099, -0.096		-0.724, 0.282
LS Mean Diff. to Placebo [2]		-0.377		
LS SE Diff. to Placebo [2]		0.3572		
95% CI [2]		-1.092, 0.339		
One-sided p-value [2]		0.1481		
Hedge's G (95% CI)		-0.39 [-1.138, 0.361]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 17				
n (%)	15 (21.4)	15 (21.4)	10 (13.9)	10 (13.9)
Mean	1.2	-0.4	2.1	-0.4
SD	1.82	0.79	1.84	1.29
Median	0.3	-0.3	1.7	-0.1
Min, Max	0, 6	-2, 1	0, 6	-3, 2
LS Mean [2]		-0.400		-0.406
LS SE [2]		0.2534		0.2606
95% CI [2]		-0.911, 0.111		-0.929, 0.118
LS Mean Diff. to Placebo [2]		0.005		
LS SE Diff. to Placebo [2]		0.3651		
95% CI [2]		-0.730, 0.741		
One-sided p-value [2]		0.5060		
Hedge's G (95% CI)		0.01 [-0.794, 0.806]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 18				
n (%)	14 (20.0)	14 (20.0)	10 (13.9)	10 (13.9)
Mean	1.2	-0.5	2.2	-0.7
SD	1.81	0.78	2.12	2.08
Median	0.5	-0.3	2.0	-0.4
Min, Max	0, 6	-2, 0	0, 7	-6, 2
LS Mean [2]		-0.471		-0.271
LS SE [2]		0.2654		0.2767
95% CI [2]		-1.004, 0.063		-0.825, 0.283
LS Mean Diff. to Placebo [2]		-0.200		
LS SE Diff. to Placebo [2]		0.3853		
95% CI [2]		-0.973, 0.574		
One-sided p-value [2]		0.3032		
Hedge's G (95% CI)		-0.20 [-1.017, 0.610]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 19				
n (%)	15 (21.4)	15 (21.4)	10 (13.9)	10 (13.9)
Mean	1.3	-0.3	2.0	-0.7
SD	1.62	0.91	1.92	2.13
Median	0.7	0.0	1.9	-0.2
Min, Max	0, 6	-2, 1	0, 6	-6, 2
LS Mean [2]		-0.331		-0.184
LS SE [2]		0.2593		0.2747
95% CI [2]		-0.853, 0.190		-0.735, 0.367
LS Mean Diff. to Placebo [2]		-0.147		
LS SE Diff. to Placebo [2]		0.3798		
95% CI [2]		-0.910, 0.615		
One-sided p-value [2]		0.3497		
Hedge's G (95% CI)		-0.15 [-0.951, 0.652]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Cycle 20				
n (%)	13 (18.6)	13 (18.6)	8 (11.1)	8 (11.1)
Mean	1.0	-0.4	1.8	-1.3
SD	1.28	1.17	2.37	2.28
Median	0.3	0.0	1.4	-0.6
Min, Max	0, 4	-3, 1	0, 7	-6, 1
Cycle 21				
n (%)	14 (20.0)	14 (20.0)	7 (9.7)	7 (9.7)
Mean	1.0	-0.4	1.9	-1.2
SD	1.57	0.83	2.33	2.55
Median	0.6	-0.1	1.3	-1.0
Min, Max	0, 6	-2, 1	0, 6	-6, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Cycle 22				
n (%)	13 (18.6)	13 (18.6)	9 (12.5)	9 (12.5)
Mean	0.5	-0.5	1.9	-1.1
SD	0.71	0.88	1.97	1.92
Median	0.2	-0.1	1.1	-1.0
Min, Max	0, 2	-2, 1	0, 6	-5, 2
Cycle 23				
n (%)	13 (18.6)	13 (18.6)	9 (12.5)	9 (12.5)
Mean	1.2	-0.2	2.3	-0.1
SD	1.72	0.85	1.77	1.26
Median	0.6	0.0	2.3	0.0
Min, Max	0, 6	-2, 1	0, 5	-2, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Cycle 24				
n (%)	9 (12.9)	9 (12.9)	6 (8.3)	6 (8.3)
Mean	0.8	-0.5	1.6	-1.1
SD	1.92	0.88	1.71	2.33
Median	0.0	-0.1	1.2	-0.8
Min, Max	0, 6	-2, 0	0, 4	-5, 2
Cycle 25				
n (%)	8 (11.4)	8 (11.4)	3 (4.2)	3 (4.2)
Mean	0.2	-0.6	1.6	-2.9
SD	0.28	0.90	0.68	1.85
Median	0.0	-0.2	1.2	-1.9
Min, Max	0, 1	-2, 0	1, 2	-5, -2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Cycle 26				
n (%)	4 (5.7)	4 (5.7)	1 (1.4)	1 (1.4)
Mean	0.1	-0.9	1.2	-5.0
SD	0.13	0.98	NA	NA
Median	0.1	-0.8	1.2	-5.0
Min, Max	0, 0	-2, 0	1, 1	-5, -5
Cycle 27				
n (%)	4 (5.7)	4 (5.7)	1 (1.4)	1 (1.4)
Mean	0.1	-1.0	0.7	-5.6
SD	0.07	1.11	NA	NA
Median	0.1	-0.7	0.7	-5.6
Min, Max	0, 0	-2, 0	1, 1	-6, -6

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Cycle 28				
n (%)	4 (5.7)	4 (5.7)	1 (1.4)	1 (1.4)
Mean	0.2	-1.2	0.4	-5.9
SD	0.35	0.83	NA	NA
Median	0.1	-1.0	0.4	-5.9
Min, Max	0, 1	-2, 0	0, 0	-6, -6
Cycle 29				
n (%)	3 (4.3)	3 (4.3)	1 (1.4)	1 (1.4)
Mean	0.1	-1.3	0.5	-5.8
SD	0.10	1.08	NA	NA
Median	0.0	-1.2	0.5	-5.8
Min, Max	0, 0	-2, 0	0, 0	-6, -6

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Cycle 30				
n (%)	4 (5.7)	4 (5.7)	3 (4.2)	3 (4.2)
Mean	0.1	-1.3	1.1	-2.9
SD	0.10	0.84	0.79	2.34
Median	0.1	-1.2	0.7	-2.1
Min, Max	0, 0	-2, 0	1, 2	-6, -1
Cycle 31				
n (%)	3 (4.3)	3 (4.3)	3 (4.2)	3 (4.2)
Mean	0.0	-1.3	1.5	-2.6
SD	0.06	1.02	1.27	2.75
Median	0.0	-1.3	1.0	-1.2
Min, Max	0, 0	-2, 0	1, 3	-6, -1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Abdominal Symptoms Domain				
Cycle 32				
n (%)	2 (2.9)	2 (2.9)	0	0
Mean	0.0	-1.9		
SD	0.05	0.86		
Median	0.0	-1.9		
Min, Max	0, 0	-2, -1		
Cycle 33				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.3	-2.1		
SD	NA	NA		
Median	0.3	-2.1		
Min, Max	0, 0	-2, -2		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Abdominal Symptoms Domain				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	3.5	0.2		
SD	NA	NA		
Median	3.5	0.2		
Min, Max	3, 3	0, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	3.2		3.5	
SD	2.44		2.78	
Median	2.7		2.7	
Min, Max	0, 9		0, 10	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Effect over Study Duration				
n (%)		67 (95.7)		69 (95.8)
LS Mean [2]		-1.455		0.176
LS SE [2]		0.1990		0.2020
95% CI [2]		-1.848, -1.062		-0.223, 0.575
LS Mean Diff. to Placebo [2]		-1.631		
LS SE Diff. to Placebo [2]		0.2657		
95% CI [2]		-2.156, -1.106		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.99 [-1.342, -0.630]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	61 (84.7)	61 (84.7)
Mean	2.2	-1.1	3.4	-0.1
SD	2.24	1.62	2.75	0.99
Median	1.7	-0.7	2.7	0.0
Min, Max	0, 8	-6, 3	0, 9	-3, 2
LS Mean [2]		-1.203		-0.141
LS SE [2]		0.2318		0.2288
95% CI [2]		-1.662, -0.744		-0.594, 0.312
LS Mean Diff. to Placebo [2]		-1.062		
LS SE Diff. to Placebo [2]		0.3100		
95% CI [2]		-1.676, -0.448		
One-sided p-value [2]		0.0004		
Hedge's G (95% CI)		-0.59 [-0.953, -0.228]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 3				
n (%)	57 (81.4)	57 (81.4)	62 (86.1)	62 (86.1)
Mean	2.2	-1.2	3.5	0.1
SD	2.42	1.67	2.81	1.37
Median	1.6	-0.8	2.8	0.1
Min, Max	0, 9	-6, 3	0, 10	-3, 4
LS Mean [2]		-1.301		0.088
LS SE [2]		0.2650		0.2597
95% CI [2]		-1.825, -0.777		-0.426, 0.602
LS Mean Diff. to Placebo [2]		-1.389		
LS SE Diff. to Placebo [2]		0.3575		
95% CI [2]		-2.097, -0.681		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.69 [-1.056, -0.316]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 4				
n (%)	44 (62.9)	44 (62.9)	43 (59.7)	43 (59.7)
Mean	1.6	-1.7	3.6	0.4
SD	1.91	2.02	2.87	1.20
Median	0.9	-1.3	3.3	0.2
Min, Max	0, 8	-7, 2	0, 10	-2, 5
LS Mean [2]		-1.367		0.234
LS SE [2]		0.2936		0.2891
95% CI [2]		-1.948, -0.785		-0.339, 0.806
LS Mean Diff. to Placebo [2]		-1.601		
LS SE Diff. to Placebo [2]		0.3995		
95% CI [2]		-2.392, -0.809		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.83 [-1.271, -0.395]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 5				
n (%)	45 (64.3)	45 (64.3)	46 (63.9)	45 (62.5)
Mean	1.7	-1.6	3.2	-0.1
SD	1.89	1.93	2.83	1.80
Median	1.0	-1.2	2.6	0.0
Min, Max	0, 7	-6, 2	0, 10	-6, 4
LS Mean [2]		-1.388		0.015
LS SE [2]		0.2819		0.2775
95% CI [2]		-1.946, -0.830		-0.534, 0.564
LS Mean Diff. to Placebo [2]		-1.403		
LS SE Diff. to Placebo [2]		0.3829		
95% CI [2]		-2.161, -0.645		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-0.75 [-1.175, -0.320]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 6				
n (%)	47 (67.1)	47 (67.1)	46 (63.9)	46 (63.9)
Mean	1.9	-1.3	3.2	0.0
SD	2.08	1.75	2.83	1.69
Median	1.2	-1.2	2.4	0.0
Min, Max	0, 8	-5, 3	0, 10	-5, 5
LS Mean [2]		-1.274		-0.012
LS SE [2]		0.2499		0.2466
95% CI [2]		-1.769, -0.780		-0.500, 0.476
LS Mean Diff. to Placebo [2]		-1.262		
LS SE Diff. to Placebo [2]		0.3366		
95% CI [2]		-1.928, -0.596		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		-0.75 [-1.166, -0.325]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 7				
n (%)	45 (64.3)	45 (64.3)	40 (55.6)	40 (55.6)
Mean	2.0	-1.1	3.6	0.0
SD	2.12	1.75	3.07	1.70
Median	1.4	-0.8	2.8	0.2
Min, Max	0, 8	-5, 3	0, 10	-4, 5
LS Mean [2]		-1.151		0.112
LS SE [2]		0.2534		0.2517
95% CI [2]		-1.652, -0.650		-0.386, 0.609
LS Mean Diff. to Placebo [2]		-1.262		
LS SE Diff. to Placebo [2]		0.3431		
95% CI [2]		-1.941, -0.583		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-0.77 [-1.206, -0.324]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 8				
n (%)	40 (57.1)	40 (57.1)	35 (48.6)	35 (48.6)
Mean	2.1	-1.6	3.6	0.1
SD	2.24	1.87	2.79	1.87
Median	1.5	-1.3	3.3	0.0
Min, Max	0, 8	-6, 2	0, 10	-4, 4
LS Mean [2]		-1.397		0.149
LS SE [2]		0.2384		0.2374
95% CI [2]		-1.869, -0.926		-0.320, 0.619
LS Mean Diff. to Placebo [2]		-1.547		
LS SE Diff. to Placebo [2]		0.3218		
95% CI [2]		-2.183, -0.910		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.06 [-1.543, -0.575]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 9				
n (%)	41 (58.6)	41 (58.6)	31 (43.1)	31 (43.1)
Mean	1.8	-1.7	4.1	0.2
SD	2.05	1.90	2.89	1.85
Median	1.4	-1.3	3.4	0.2
Min, Max	0, 8	-6, 1	0, 10	-4, 4
LS Mean [2]		-1.471		0.421
LS SE [2]		0.2368		0.2398
95% CI [2]		-1.939, -1.003		-0.052, 0.895
LS Mean Diff. to Placebo [2]		-1.893		
LS SE Diff. to Placebo [2]		0.3220		
95% CI [2]		-2.529, -1.256		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.31 [-1.827, -0.800]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 10				
n (%)	40 (57.1)	40 (57.1)	32 (44.4)	32 (44.4)
Mean	1.7	-1.7	4.2	0.5
SD	1.99	1.80	3.07	2.26
Median	1.0	-1.5	3.5	0.3
Min, Max	0, 8	-6, 2	0, 10	-5, 6
LS Mean [2]		-1.384		0.410
LS SE [2]		0.2469		0.2506
95% CI [2]		-1.872, -0.897		-0.085, 0.905
LS Mean Diff. to Placebo [2]		-1.794		
LS SE Diff. to Placebo [2]		0.3375		
95% CI [2]		-2.462, -1.127		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.20 [-1.701, -0.692]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 11				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	1.8	-1.6	3.7	0.2
SD	1.82	1.89	2.90	1.75
Median	1.3	-1.2	3.1	0.3
Min, Max	0, 7	-6, 1	0, 10	-4, 5
LS Mean [2]		-1.461		0.219
LS SE [2]		0.2192		0.2254
95% CI [2]		-1.895, -1.028		-0.227, 0.664
LS Mean Diff. to Placebo [2]		-1.680		
LS SE Diff. to Placebo [2]		0.2983		
95% CI [2]		-2.270, -1.090		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.31 [-1.842, -0.769]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 12				
n (%)	40 (57.1)	40 (57.1)	26 (36.1)	26 (36.1)
Mean	1.6	-1.7	3.4	-0.3
SD	1.72	1.78	2.84	2.05
Median	1.4	-1.3	3.0	0.0
Min, Max	0, 7	-7, 1	0, 10	-4, 5
LS Mean [2]		-1.514		0.163
LS SE [2]		0.2172		0.2273
95% CI [2]		-1.943, -1.084		-0.285, 0.612
LS Mean Diff. to Placebo [2]		-1.677		
LS SE Diff. to Placebo [2]		0.2981		
95% CI [2]		-2.266, -1.088		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.30 [-1.837, -0.755]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	1.8	-1.7	3.8	0.1
SD	1.84	1.84	2.86	1.94
Median	1.3	-1.4	3.6	0.0
Min, Max	0, 7	-6, 1	0, 10	-4, 5
LS Mean [2]		-1.413		0.274
LS SE [2]		0.2166		0.2287
95% CI [2]		-1.842, -0.985		-0.178, 0.725
LS Mean Diff. to Placebo [2]		-1.687		
LS SE Diff. to Placebo [2]		0.2988		
95% CI [2]		-2.277, -1.096		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.39 [-1.975, -0.808]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 14				
n (%)	35 (50.0)	35 (50.0)	25 (34.7)	25 (34.7)
Mean	1.7	-1.7	3.9	0.2
SD	1.91	1.94	3.16	1.98
Median	1.0	-1.2	2.9	0.0
Min, Max	0, 7	-7, 1	0, 10	-4, 5
LS Mean [2]		-1.523		0.333
LS SE [2]		0.2221		0.2338
95% CI [2]		-1.962, -1.084		-0.128, 0.795
LS Mean Diff. to Placebo [2]		-1.856		
LS SE Diff. to Placebo [2]		0.3067		
95% CI [2]		-2.462, -1.251		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.48 [-2.055, -0.900]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 15				
n (%)	39 (55.7)	39 (55.7)	23 (31.9)	23 (31.9)
Mean	1.9	-1.7	3.8	-0.1
SD	1.82	1.72	3.30	2.27
Median	1.6	-1.4	2.9	0.0
Min, Max	0, 7	-6, 1	0, 10	-6, 4
LS Mean [2]		-1.475		0.235
LS SE [2]		0.2116		0.2265
95% CI [2]		-1.892, -1.057		-0.212, 0.682
LS Mean Diff. to Placebo [2]		-1.710		
LS SE Diff. to Placebo [2]		0.2933		
95% CI [2]		-2.289, -1.130		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.38 [-1.948, -0.809]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 16				
n (%)	38 (54.3)	38 (54.3)	25 (34.7)	25 (34.7)
Mean	1.7	-1.7	3.4	-0.3
SD	1.83	1.82	2.99	2.43
Median	1.2	-1.4	2.8	0.0
Min, Max	0, 8	-6, 2	0, 10	-7, 4
LS Mean [2]		-1.502		-0.008
LS SE [2]		0.2159		0.2306
95% CI [2]		-1.928, -1.076		-0.463, 0.447
LS Mean Diff. to Placebo [2]		-1.494		
LS SE Diff. to Placebo [2]		0.2998		
95% CI [2]		-2.086, -0.902		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.18 [-1.727, -0.637]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 17				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	1.7	-1.8	3.7	0.7
SD	1.79	1.48	3.06	1.68
Median	1.1	-1.6	3.3	0.4
Min, Max	0, 7	-6, 1	0, 10	-3, 4
LS Mean [2]		-1.642		0.273
LS SE [2]		0.1996		0.2161
95% CI [2]		-2.037, -1.248		-0.154, 0.699
LS Mean Diff. to Placebo [2]		-1.915		
LS SE Diff. to Placebo [2]		0.2772		
95% CI [2]		-2.463, -1.367		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.73 [-2.353, -1.104]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	21 (29.2)
Mean	1.6	-1.8	3.6	0.4
SD	1.56	1.87	3.18	2.25
Median	1.2	-1.2	3.7	0.3
Min, Max	0, 5	-6, 2	0, 10	-4, 5
LS Mean [2]		-1.591		0.281
LS SE [2]		0.2204		0.2406
95% CI [2]		-2.026, -1.155		-0.194, 0.755
LS Mean Diff. to Placebo [2]		-1.871		
LS SE Diff. to Placebo [2]		0.3106		
95% CI [2]		-2.485, -1.258		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.55 [-2.172, -0.931]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	23 (31.9)	23 (31.9)
Mean	1.7	-1.5	2.9	0.0
SD	1.62	1.69	2.48	2.30
Median	1.4	-1.3	2.2	0.3
Min, Max	0, 5	-6, 2	0, 8	-5, 4
LS Mean [2]		-1.472		0.149
LS SE [2]		0.2168		0.2386
95% CI [2]		-1.900, -1.044		-0.321, 0.620
LS Mean Diff. to Placebo [2]		-1.622		
LS SE Diff. to Placebo [2]		0.3063		
95% CI [2]		-2.227, -1.017		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.33 [-1.915, -0.749]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 20				
n (%)	33 (47.1)	33 (47.1)	17 (23.6)	17 (23.6)
Mean	1.7	-1.6	3.1	-0.4
SD	1.67	2.04	2.69	2.33
Median	1.6	-1.5	2.6	-0.1
Min, Max	0, 6	-7, 4	0, 8	-5, 3
LS Mean [2]		-1.438		0.206
LS SE [2]		0.2271		0.2584
95% CI [2]		-1.886, -0.989		-0.303, 0.716
LS Mean Diff. to Placebo [2]		-1.644		
LS SE Diff. to Placebo [2]		0.3296		
95% CI [2]		-2.295, -0.993		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.34 [-1.978, -0.696]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 21				
n (%)	35 (50.0)	35 (50.0)	14 (19.4)	14 (19.4)
Mean	1.6	-1.7	3.4	0.0
SD	1.81	1.48	2.77	2.25
Median	1.2	-1.8	3.3	0.1
Min, Max	0, 7	-5, 1	0, 8	-4, 4
LS Mean [2]		-1.590		0.158
LS SE [2]		0.2049		0.2390
95% CI [2]		-1.994, -1.185		-0.313, 0.630
LS Mean Diff. to Placebo [2]		-1.748		
LS SE Diff. to Placebo [2]		0.2993		
95% CI [2]		-2.339, -1.157		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.52 [-2.206, -0.829]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 22				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	1.3	-1.7	3.2	-0.3
SD	1.51	1.58	2.60	2.28
Median	1.0	-1.7	2.5	-0.3
Min, Max	0, 5	-5, 2	0, 8	-4, 3
LS Mean [2]		-1.638		0.178
LS SE [2]		0.2100		0.2397
95% CI [2]		-2.052, -1.223		-0.295, 0.652
LS Mean Diff. to Placebo [2]		-1.816		
LS SE Diff. to Placebo [2]		0.3031		
95% CI [2]		-2.415, -1.217		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.60 [-2.243, -0.950]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 23				
n (%)	30 (42.9)	30 (42.9)	15 (20.8)	15 (20.8)
Mean	1.7	-1.5	2.7	0.2
SD	1.87	1.73	2.72	1.95
Median	1.2	-1.4	1.9	0.1
Min, Max	0, 8	-5, 2	0, 8	-3, 3
LS Mean [2]		-1.643		0.187
LS SE [2]		0.2216		0.2607
95% CI [2]		-2.081, -1.205		-0.328, 0.702
LS Mean Diff. to Placebo [2]		-1.830		
LS SE Diff. to Placebo [2]		0.3269		
95% CI [2]		-2.476, -1.184		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.56 [-2.260, -0.863]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 24				
n (%)	23 (32.9)	23 (32.9)	12 (16.7)	12 (16.7)
Mean	1.7	-1.5	3.3	0.0
SD	1.97	1.55	2.82	2.01
Median	1.5	-1.5	3.0	0.1
Min, Max	0, 7	-4, 2	0, 8	-3, 3
LS Mean [2]		-1.624		0.121
LS SE [2]		0.2131		0.2509
95% CI [2]		-2.045, -1.202		-0.375, 0.618
LS Mean Diff. to Placebo [2]		-1.745		
LS SE Diff. to Placebo [2]		0.3148		
95% CI [2]		-2.368, -1.122		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.75 [-2.561, -0.942]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 25				
n (%)	21 (30.0)	21 (30.0)	6 (8.3)	6 (8.3)
Mean	1.5	-1.6	5.1	-0.2
SD	1.94	1.70	3.25	2.12
Median	0.5	-1.3	6.2	-0.7
Min, Max	0, 7	-5, 2	1, 8	-2, 3
Cycle 26				
n (%)	13 (18.6)	13 (18.6)	4 (5.6)	4 (5.6)
Mean	1.8	-1.5	6.5	0.5
SD	2.17	1.84	2.64	1.56
Median	1.1	-1.2	7.8	1.0
Min, Max	0, 7	-5, 2	3, 8	-2, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 27				
n (%)	14 (20.0)	14 (20.0)	3 (4.2)	3 (4.2)
Mean	2.0	-1.4	5.6	-0.2
SD	2.17	1.76	3.00	2.42
Median	1.4	-1.2	6.6	0.8
Min, Max	0, 7	-5, 2	2, 8	-3, 2
Cycle 28				
n (%)	16 (22.9)	16 (22.9)	3 (4.2)	3 (4.2)
Mean	1.9	-1.7	5.2	0.8
SD	2.03	1.76	2.35	3.03
Median	1.6	-1.8	5.9	1.1
Min, Max	0, 7	-5, 2	3, 7	-2, 4

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 29				
n (%)	13 (18.6)	13 (18.6)	3 (4.2)	3 (4.2)
Mean	1.8	-1.9	5.1	0.8
SD	2.00	1.87	2.53	2.66
Median	1.3	-1.2	5.4	1.4
Min, Max	0, 6	-5, 1	2, 7	-2, 3
Cycle 30				
n (%)	12 (17.1)	12 (17.1)	5 (6.9)	5 (6.9)
Mean	1.3	-2.0	3.7	-0.6
SD	1.63	1.74	2.73	2.76
Median	0.7	-1.9	2.7	-2.0
Min, Max	0, 5	-5, 1	1, 7	-3, 3

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 31				
n (%)	9 (12.9)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	1.6	-2.0	4.2	-0.9
SD	2.31	2.28	2.56	3.16
Median	1.6	-2.7	4.3	-2.4
Min, Max	0, 7	-5, 1	2, 7	-3, 4
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	1.7	-1.0	4.5	2.6
SD	2.48	1.54	2.96	2.44
Median	0.9	-0.7	4.5	2.6
Min, Max	0, 6	-3, 1	2, 7	1, 4

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 33				
n (%)	6 (8.6)	6 (8.6)	0	0
Mean	1.8	-2.2		
SD	2.50	2.47		
Median	1.0	-2.7		
Min, Max	0, 6	-5, 1		
Cycle 34				
n (%)	4 (5.7)	4 (5.7)	0	0
Mean	1.6	-2.5		
SD	3.20	2.25		
Median	0.0	-2.4		
Min, Max	0, 6	-5, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.1	-2.0		
SD	NA	NA		
Median	0.1	-2.0		
Min, Max	0, 0	-2, -2		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.1		
SD	NA	NA		
Median	0.0	-2.1		
Min, Max	0, 0	-2, -2		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Extra-Abdominal Symptoms Domain				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	0.0		
SD	NA	NA		
Median	0.0	0.0		
Min, Max	0, 0	0, 0		
Follow-Up				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	2.8	-0.9		
SD	3.09	2.77		
Median	1.6	0.2		
Min, Max	0, 7	-6, 1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	3.4		3.6	
SD	2.33		2.58	
Median	3.2		3.1	
Min, Max	0, 8		0, 9	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Effect over Study Duration				
n (%)		67 (95.7)		69 (95.8)
LS Mean [2]		-1.410		0.156
LS SE [2]		0.1841		0.1866
95% CI [2]		-1.774, -1.046		-0.213, 0.524
LS Mean Diff. to Placebo [2]		-1.566		
LS SE Diff. to Placebo [2]		0.2465		
95% CI [2]		-2.053, -1.079		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.02 [-1.381, -0.666]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	61 (84.7)	61 (84.7)
Mean	2.3	-1.1	3.4	-0.2
SD	2.09	1.54	2.50	1.07
Median	1.8	-0.8	2.8	0.0
Min, Max	0, 8	-6, 2	0, 8	-3, 2
LS Mean [2]		-1.136		-0.148
LS SE [2]		0.2072		0.2048
95% CI [2]		-1.546, -0.726		-0.553, 0.258
LS Mean Diff. to Placebo [2]		-0.989		
LS SE Diff. to Placebo [2]		0.2773		
95% CI [2]		-1.538, -0.439		
One-sided p-value [2]		0.0003		
Hedge's G (95% CI)		-0.61 [-0.978, -0.251]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 3				
n (%)	57 (81.4)	57 (81.4)	62 (86.1)	62 (86.1)
Mean	2.2	-1.3	3.5	0.0
SD	2.16	1.61	2.54	1.31
Median	1.6	-1.0	3.1	0.0
Min, Max	0, 9	-6, 2	0, 9	-3, 4
LS Mean [2]		-1.302		0.069
LS SE [2]		0.2319		0.2274
95% CI [2]		-1.761, -0.843		-0.381, 0.519
LS Mean Diff. to Placebo [2]		-1.371		
LS SE Diff. to Placebo [2]		0.3124		
95% CI [2]		-1.989, -0.752		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.77 [-1.147, -0.401]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 4				
n (%)	44 (62.9)	44 (62.9)	43 (59.7)	43 (59.7)
Mean	1.7	-1.6	3.7	0.3
SD	1.77	1.95	2.68	1.12
Median	1.1	-1.3	3.7	0.1
Min, Max	0, 8	-7, 2	0, 10	-2, 4
LS Mean [2]		-1.379		0.244
LS SE [2]		0.2549		0.2514
95% CI [2]		-1.883, -0.874		-0.254, 0.742
LS Mean Diff. to Placebo [2]		-1.622		
LS SE Diff. to Placebo [2]		0.3466		
95% CI [2]		-2.309, -0.936		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.97 [-1.416, -0.527]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 5				
n (%)	45 (64.3)	45 (64.3)	46 (63.9)	45 (62.5)
Mean	1.8	-1.5	3.4	-0.1
SD	1.72	1.71	2.52	1.62
Median	1.3	-1.1	3.0	0.0
Min, Max	0, 7	-6, 2	0, 9	-5, 3
LS Mean [2]		-1.318		0.077
LS SE [2]		0.2439		0.2401
95% CI [2]		-1.801, -0.835		-0.398, 0.553
LS Mean Diff. to Placebo [2]		-1.395		
LS SE Diff. to Placebo [2]		0.3305		
95% CI [2]		-2.050, -0.741		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.86 [-1.291, -0.428]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
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Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 6				
n (%)	47 (67.1)	47 (67.1)	46 (63.9)	46 (63.9)
Mean	1.9	-1.4	3.3	0.0
SD	2.01	1.84	2.50	1.53
Median	1.2	-1.1	2.7	0.0
Min, Max	0, 9	-5, 4	0, 9	-4, 5
LS Mean [2]		-1.256		0.065
LS SE [2]		0.2359		0.2330
95% CI [2]		-1.723, -0.790		-0.396, 0.526
LS Mean Diff. to Placebo [2]		-1.322		
LS SE Diff. to Placebo [2]		0.3193		
95% CI [2]		-1.953, -0.690		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.83 [-1.250, -0.403]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
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[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 7				
n (%)	45 (64.3)	45 (64.3)	40 (55.6)	40 (55.6)
Mean	2.0	-1.2	3.5	-0.1
SD	1.89	1.62	2.81	1.49
Median	1.4	-1.1	2.8	0.1
Min, Max	0, 8	-5, 2	0, 10	-3, 3
LS Mean [2]		-1.166		0.106
LS SE [2]		0.2311		0.2301
95% CI [2]		-1.623, -0.709		-0.349, 0.561
LS Mean Diff. to Placebo [2]		-1.272		
LS SE Diff. to Placebo [2]		0.3139		
95% CI [2]		-1.894, -0.651		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.84 [-1.289, -0.400]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 8				
n (%)	40 (57.1)	40 (57.1)	35 (48.6)	35 (48.6)
Mean	2.1	-1.6	3.7	0.1
SD	2.11	1.73	2.59	1.67
Median	1.7	-1.5	3.4	0.1
Min, Max	0, 8	-5, 2	0, 10	-3, 4
LS Mean [2]		-1.281		0.204
LS SE [2]		0.2206		0.2204
95% CI [2]		-1.717, -0.845		-0.232, 0.639
LS Mean Diff. to Placebo [2]		-1.484		
LS SE Diff. to Placebo [2]		0.2990		
95% CI [2]		-2.076, -0.893		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.10 [-1.583, -0.610]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 9				
n (%)	41 (58.6)	41 (58.6)	31 (43.1)	31 (43.1)
Mean	1.9	-1.7	4.2	0.1
SD	1.96	1.67	2.66	1.58
Median	1.2	-1.5	3.4	0.1
Min, Max	0, 8	-6, 1	0, 10	-4, 3
LS Mean [2]		-1.375		0.406
LS SE [2]		0.2169		0.2206
95% CI [2]		-1.804, -0.946		-0.030, 0.842
LS Mean Diff. to Placebo [2]		-1.781		
LS SE Diff. to Placebo [2]		0.2962		
95% CI [2]		-2.367, -1.195		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.35 [-1.863, -0.831]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 10				
n (%)	40 (57.1)	40 (57.1)	32 (44.4)	32 (44.4)
Mean	1.7	-1.7	4.1	0.3
SD	1.81	1.59	2.69	1.95
Median	1.0	-1.8	4.0	0.2
Min, Max	0, 7	-6, 1	0, 9	-5, 5
LS Mean [2]		-1.350		0.380
LS SE [2]		0.2233		0.2272
95% CI [2]		-1.792, -0.909		-0.069, 0.829
LS Mean Diff. to Placebo [2]		-1.730		
LS SE Diff. to Placebo [2]		0.3058		
95% CI [2]		-2.335, -1.125		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.27 [-1.784, -0.765]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 11				
n (%)	38 (54.3)	38 (54.3)	28 (38.9)	28 (38.9)
Mean	1.7	-1.6	3.5	0.0
SD	1.76	1.63	2.30	1.36
Median	1.3	-1.3	2.9	0.1
Min, Max	0, 7	-6, 1	0, 9	-3, 3
LS Mean [2]		-1.466		0.162
LS SE [2]		0.1913		0.1973
95% CI [2]		-1.844, -1.087		-0.228, 0.552
LS Mean Diff. to Placebo [2]		-1.628		
LS SE Diff. to Placebo [2]		0.2597		
95% CI [2]		-2.141, -1.114		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.45 [-1.995, -0.901]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 12				
n (%)	40 (57.1)	40 (57.1)	26 (36.1)	26 (36.1)
Mean	1.8	-1.6	3.4	-0.4
SD	1.71	1.58	2.34	1.67
Median	1.4	-1.4	2.9	-0.5
Min, Max	0, 7	-5, 1	0, 10	-4, 4
LS Mean [2]		-1.390		0.211
LS SE [2]		0.1983		0.2084
95% CI [2]		-1.782, -0.997		-0.201, 0.622
LS Mean Diff. to Placebo [2]		-1.600		
LS SE Diff. to Placebo [2]		0.2733		
95% CI [2]		-2.141, -1.060		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.35 [-1.897, -0.807]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	1.8	-1.8	3.6	-0.1
SD	1.83	1.67	2.45	1.76
Median	1.4	-1.8	3.2	0.0
Min, Max	0, 7	-6, 1	0, 9	-4, 3
LS Mean [2]		-1.395		0.281
LS SE [2]		0.2086		0.2207
95% CI [2]		-1.807, -0.982		-0.155, 0.717
LS Mean Diff. to Placebo [2]		-1.676		
LS SE Diff. to Placebo [2]		0.2902		
95% CI [2]		-2.250, -1.102		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.43 [-2.022, -0.847]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 14				
n (%)	35 (50.0)	35 (50.0)	25 (34.7)	25 (34.7)
Mean	1.7	-1.7	3.7	0.0
SD	1.85	1.65	2.66	1.72
Median	1.4	-1.5	3.0	0.1
Min, Max	0, 7	-7, 1	0, 9	-3, 3
LS Mean [2]		-1.471		0.258
LS SE [2]		0.2086		0.2199
95% CI [2]		-1.883, -1.058		-0.176, 0.692
LS Mean Diff. to Placebo [2]		-1.729		
LS SE Diff. to Placebo [2]		0.2896		
95% CI [2]		-2.302, -1.156		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.46 [-2.041, -0.888]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 15				
n (%)	39 (55.7)	39 (55.7)	23 (31.9)	23 (31.9)
Mean	1.9	-1.7	3.7	-0.4
SD	1.85	1.51	2.68	1.90
Median	1.5	-1.7	3.3	0.0
Min, Max	0, 7	-5, 1	0, 9	-5, 3
LS Mean [2]		-1.472		0.126
LS SE [2]		0.1920		0.2062
95% CI [2]		-1.852, -1.093		-0.281, 0.533
LS Mean Diff. to Placebo [2]		-1.599		
LS SE Diff. to Placebo [2]		0.2669		
95% CI [2]		-2.126, -1.072		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.42 [-1.992, -0.847]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 16				
n (%)	38 (54.3)	38 (54.3)	25 (34.7)	25 (34.7)
Mean	1.6	-1.8	3.5	-0.3
SD	1.73	1.60	2.64	2.15
Median	1.0	-1.9	3.4	0.1
Min, Max	0, 7	-5, 1	0, 9	-6, 3
LS Mean [2]		-1.543		0.022
LS SE [2]		0.2037		0.2182
95% CI [2]		-1.945, -1.140		-0.408, 0.453
LS Mean Diff. to Placebo [2]		-1.565		
LS SE Diff. to Placebo [2]		0.2846		
95% CI [2]		-2.127, -1.003		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.31 [-1.866, -0.757]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 17				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	1.6	-1.8	3.8	0.5
SD	1.71	1.28	2.66	1.52
Median	1.2	-1.8	3.0	0.6
Min, Max	0, 7	-4, 1	0, 9	-4, 3
LS Mean [2]		-1.645		0.178
LS SE [2]		0.1935		0.2095
95% CI [2]		-2.028, -1.263		-0.235, 0.592
LS Mean Diff. to Placebo [2]		-1.824		
LS SE Diff. to Placebo [2]		0.2707		
95% CI [2]		-2.359, -1.289		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.70 [-2.320, -1.077]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	21 (29.2)
Mean	1.6	-1.8	3.7	0.2
SD	1.49	1.62	2.77	2.09
Median	1.2	-1.6	3.7	0.1
Min, Max	0, 6	-6, 1	0, 9	-4, 3
LS Mean [2]		-1.543		0.227
LS SE [2]		0.2112		0.2307
95% CI [2]		-1.960, -1.125		-0.228, 0.683
LS Mean Diff. to Placebo [2]		-1.770		
LS SE Diff. to Placebo [2]		0.2993		
95% CI [2]		-2.362, -1.178		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.53 [-2.150, -0.913]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	23 (31.9)	23 (31.9)
Mean	1.6	-1.6	2.9	-0.1
SD	1.49	1.49	2.02	2.03
Median	1.3	-1.5	3.1	0.0
Min, Max	0, 5	-5, 1	0, 7	-4, 3
LS Mean [2]		-1.448		0.012
LS SE [2]		0.1983		0.2182
95% CI [2]		-1.840, -1.056		-0.418, 0.443
LS Mean Diff. to Placebo [2]		-1.460		
LS SE Diff. to Placebo [2]		0.2803		
95% CI [2]		-2.014, -0.906		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.31 [-1.892, -0.730]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 20				
n (%)	33 (47.1)	33 (47.1)	17 (23.6)	17 (23.6)
Mean	1.7	-1.6	3.1	-0.5
SD	1.63	1.91	2.23	2.11
Median	1.4	-1.7	2.9	-0.3
Min, Max	0, 6	-5, 4	0, 7	-4, 4
LS Mean [2]		-1.295		0.241
LS SE [2]		0.2320		0.2660
95% CI [2]		-1.754, -0.836		-0.284, 0.767
LS Mean Diff. to Placebo [2]		-1.536		
LS SE Diff. to Placebo [2]		0.3418		
95% CI [2]		-2.212, -0.860		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.22 [-1.852, -0.588]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 21				
n (%)	35 (50.0)	35 (50.0)	14 (19.4)	14 (19.4)
Mean	1.7	-1.8	3.5	-0.1
SD	1.80	1.42	2.31	2.34
Median	1.4	-1.8	3.4	-0.2
Min, Max	0, 7	-4, 1	0, 7	-4, 4
LS Mean [2]		-1.532		0.087
LS SE [2]		0.1979		0.2323
95% CI [2]		-1.923, -1.141		-0.372, 0.546
LS Mean Diff. to Placebo [2]		-1.619		
LS SE Diff. to Placebo [2]		0.2920		
95% CI [2]		-2.196, -1.042		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.45 [-2.137, -0.770]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 22				
n (%)	32 (45.7)	32 (45.7)	19 (26.4)	19 (26.4)
Mean	1.3	-1.8	3.2	-0.4
SD	1.34	1.49	2.15	2.12
Median	1.2	-1.8	3.1	-0.8
Min, Max	0, 6	-5, 1	0, 7	-4, 4
LS Mean [2]		-1.585		0.008
LS SE [2]		0.1950		0.2222
95% CI [2]		-1.970, -1.199		-0.431, 0.447
LS Mean Diff. to Placebo [2]		-1.593		
LS SE Diff. to Placebo [2]		0.2820		
95% CI [2]		-2.151, -1.035		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.51 [-2.148, -0.870]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 23				
n (%)	30 (42.9)	30 (42.9)	15 (20.8)	15 (20.8)
Mean	1.7	-1.5	2.9	0.2
SD	1.77	1.54	2.15	1.93
Median	1.4	-1.5	2.9	0.2
Min, Max	0, 8	-5, 2	0, 7	-3, 4
LS Mean [2]		-1.524		0.172
LS SE [2]		0.2076		0.2443
95% CI [2]		-1.935, -1.114		-0.311, 0.655
LS Mean Diff. to Placebo [2]		-1.696		
LS SE Diff. to Placebo [2]		0.3069		
95% CI [2]		-2.303, -1.089		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.55 [-2.242, -0.848]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Total Symptom Score - Average				
Cycle 24				
n (%)	23 (32.9)	23 (32.9)	12 (16.7)	12 (16.7)
Mean	1.7	-1.5	3.3	0.0
SD	1.84	1.32	2.37	1.95
Median	1.2	-1.4	3.0	0.1
Min, Max	0, 7	-4, 1	0, 7	-3, 3
LS Mean [2]		-1.558		0.194
LS SE [2]		0.1948		0.2284
95% CI [2]		-1.944, -1.172		-0.258, 0.646
LS Mean Diff. to Placebo [2]		-1.752		
LS SE Diff. to Placebo [2]		0.2871		
95% CI [2]		-2.320, -1.183		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.92 [-2.756, -1.094]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 25				
n (%)	21 (30.0)	21 (30.0)	6 (8.3)	6 (8.3)
Mean	1.5	-1.4	4.7	-0.3
SD	1.86	1.41	2.85	1.72
Median	0.9	-1.3	5.1	-0.6
Min, Max	0, 7	-4, 1	1, 7	-2, 2
Cycle 26				
n (%)	13 (18.6)	13 (18.6)	4 (5.6)	4 (5.6)
Mean	1.8	-1.3	6.2	0.1
SD	2.10	1.52	2.36	1.29
Median	1.0	-1.2	7.3	0.2
Min, Max	0, 7	-4, 2	3, 8	-2, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 27				
n (%)	14 (20.0)	14 (20.0)	3 (4.2)	3 (4.2)
Mean	1.9	-1.3	5.9	0.3
SD	2.07	1.45	1.50	2.87
Median	1.3	-1.4	6.1	1.6
Min, Max	0, 7	-4, 2	4, 7	-3, 2
Cycle 28				
n (%)	16 (22.9)	16 (22.9)	3 (4.2)	3 (4.2)
Mean	2.0	-1.4	4.9	0.7
SD	1.88	1.42	1.03	3.25
Median	1.6	-1.3	4.5	2.5
Min, Max	0, 7	-4, 1	4, 6	-3, 3

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 29				
n (%)	13 (18.6)	13 (18.6)	3 (4.2)	3 (4.2)
Mean	1.8	-1.6	4.5	0.1
SD	1.87	1.54	1.73	2.41
Median	1.1	-1.0	3.6	0.7
Min, Max	0, 6	-4, 1	3, 7	-3, 2
Cycle 30				
n (%)	12 (17.1)	12 (17.1)	5 (6.9)	5 (6.9)
Mean	1.5	-1.6	3.7	-1.1
SD	1.58	1.41	1.77	2.36
Median	1.0	-1.3	3.2	-2.4
Min, Max	0, 5	-4, 1	2, 7	-3, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 31				
n (%)	9 (12.9)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	1.7	-1.5	3.7	-1.6
SD	2.23	1.88	1.61	2.65
Median	1.0	-0.9	3.3	-2.7
Min, Max	0, 7	-4, 1	2, 6	-3, 2
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	1.8	-0.7	4.6	2.8
SD	2.33	1.37	0.07	0.46
Median	1.1	-0.5	4.6	2.8
Min, Max	0, 6	-3, 1	5, 5	3, 3

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 33				
n (%)	6 (8.6)	6 (8.6)	0	0
Mean	2.0	-1.8		
SD	2.40	2.15		
Median	1.3	-2.0		
Min, Max	0, 7	-4, 1		
Cycle 34				
n (%)	4 (5.7)	4 (5.7)	0	0
Mean	1.8	-1.9		
SD	3.07	1.82		
Median	0.4	-1.6		
Min, Max	0, 6	-4, 0		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.4		
SD	NA	NA		
Median	0.0	-2.4		
Min, Max	0, 0	-2, -2		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.4		
SD	NA	NA		
Median	0.0	-2.4		
Min, Max	0, 0	-2, -2		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.1.1
Summary and Change from Baseline in DTSS Scores by Visit - Double-Blind Phase
Total Symptom Score, Total Symptom Score - 5 Items, Abdominal Symptoms Domain, Extra-Abdominal Symptoms Domain, Pain Domain, Total Symptom Score - Average
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Total Symptom Score - Average				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	2.3	1.1		
SD	NA	NA		
Median	2.3	1.1		
Min, Max	2, 2	1, 1		
Follow-Up				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	2.5	-1.0		
SD	2.51	2.80		
Median	1.2	0.4		
Min, Max	0, 6	-6, 1		

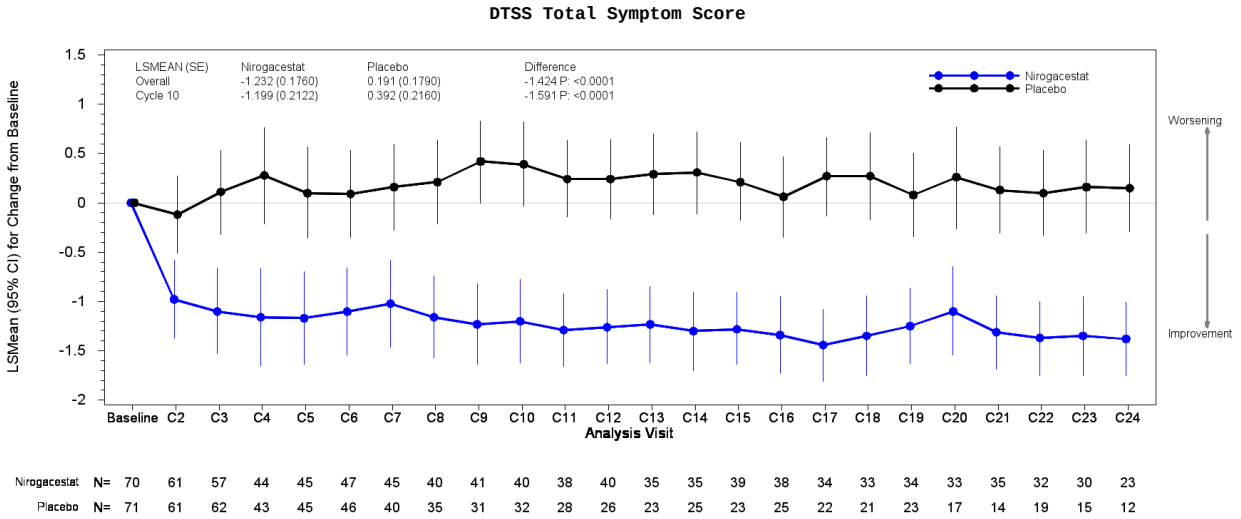
Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; DTSS = Desmoid Tumor Symptom Scale; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of symptoms and a negative change from Baseline value indicated improvement of symptoms. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the weekly average of the Baseline Period (study days -7 through -1) if there were 4 or more days of assessments during that Baseline period. If there were less than 4 days of assessments during Baseline period, the Baseline weekly score was the weekly average of the Screening visits assessments provided there were 4 or more days of assessments during that period.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline DTSS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

1.4.2 Figure MMRM DTSS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.1.2
Mixed Model Repeated Measures: Change from Baseline in DTSS Scores by Visit - Double Blind Phase
Intent-to-Treat Population

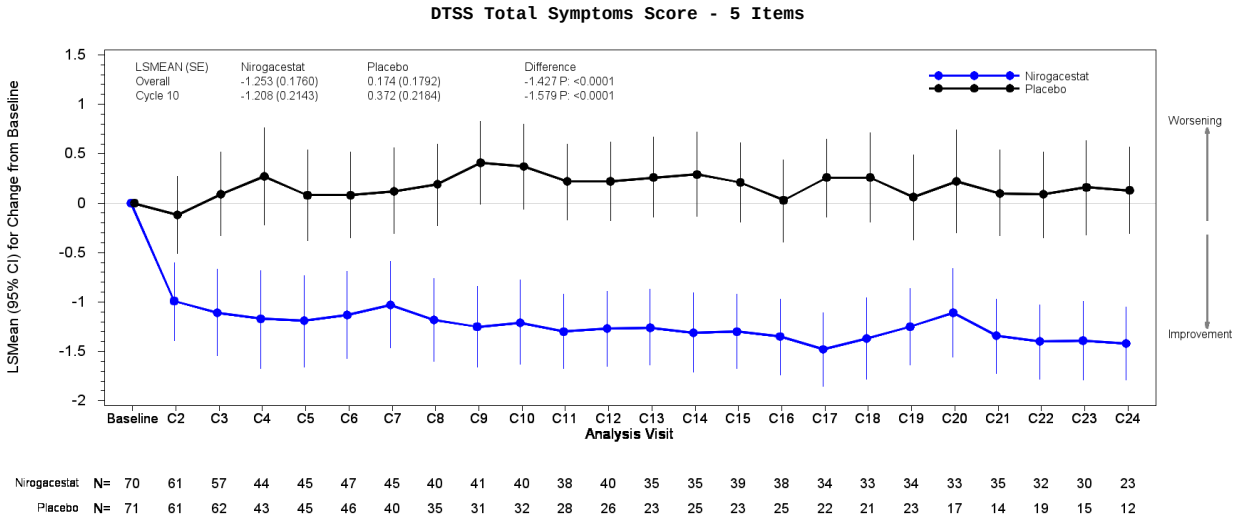


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.1.1, Dataset(s): ADSL, ADQS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.1.2
Mixed Model Repeated Measures: Change from Baseline in DTSS Scores by Visit - Double Blind Phase
Intent-to-Treat Population

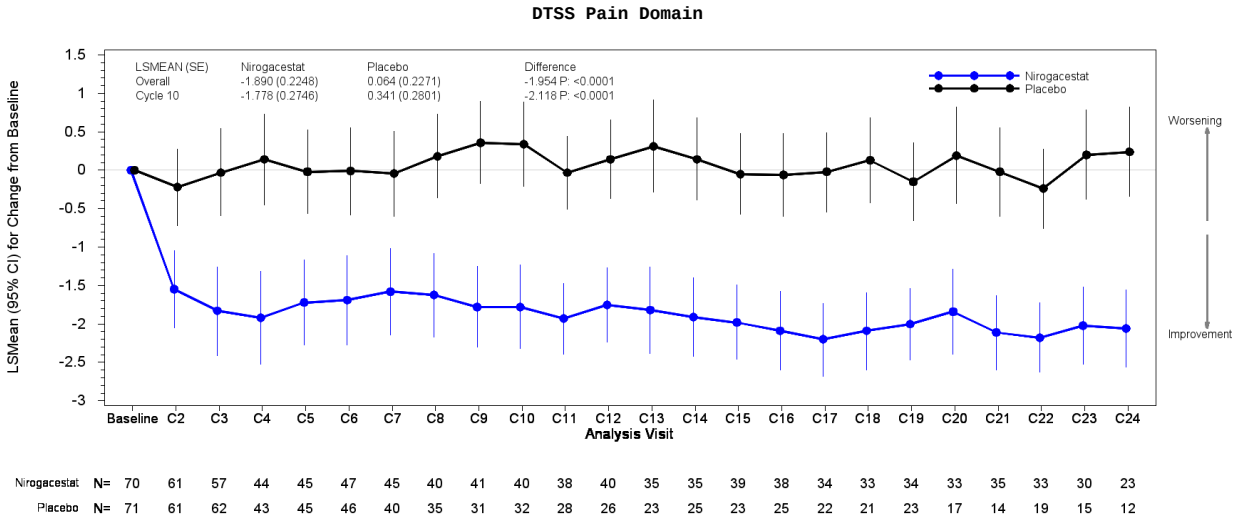


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.1.1, Dataset(s): ADSL, ADQS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.1.2
Mixed Model Repeated Measures: Change from Baseline in DTSS Scores by Visit - Double Blind Phase
Intent-to-Treat Population

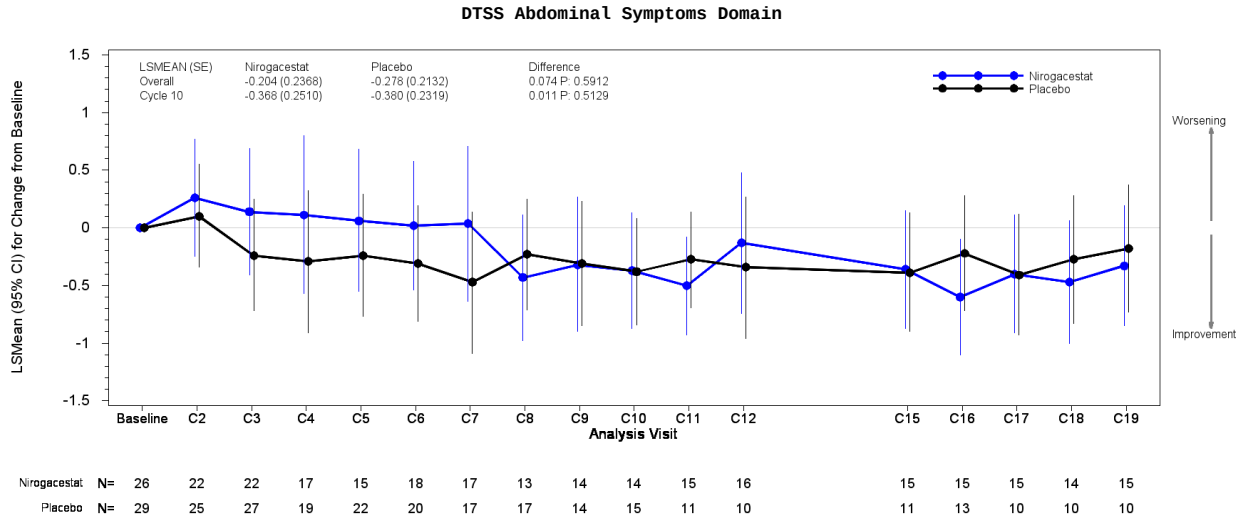


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.1.1, Dataset(s): ADSL, ADQS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.1.2
Mixed Model Repeated Measures: Change from Baseline in DTSS Scores by Visit - Double Blind Phase
Intent-to-Treat Population

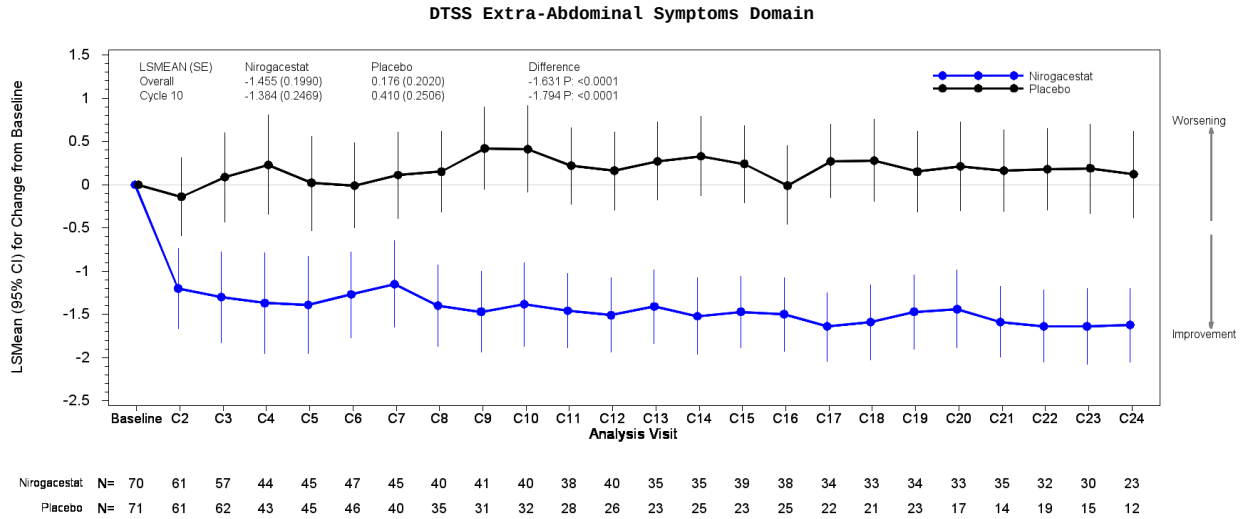


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.1.1, Dataset(s): ADSL, ADQS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.1.2
Mixed Model Repeated Measures: Change from Baseline in DTSS Scores by Visit - Double Blind Phase
Intent-to-Treat Population

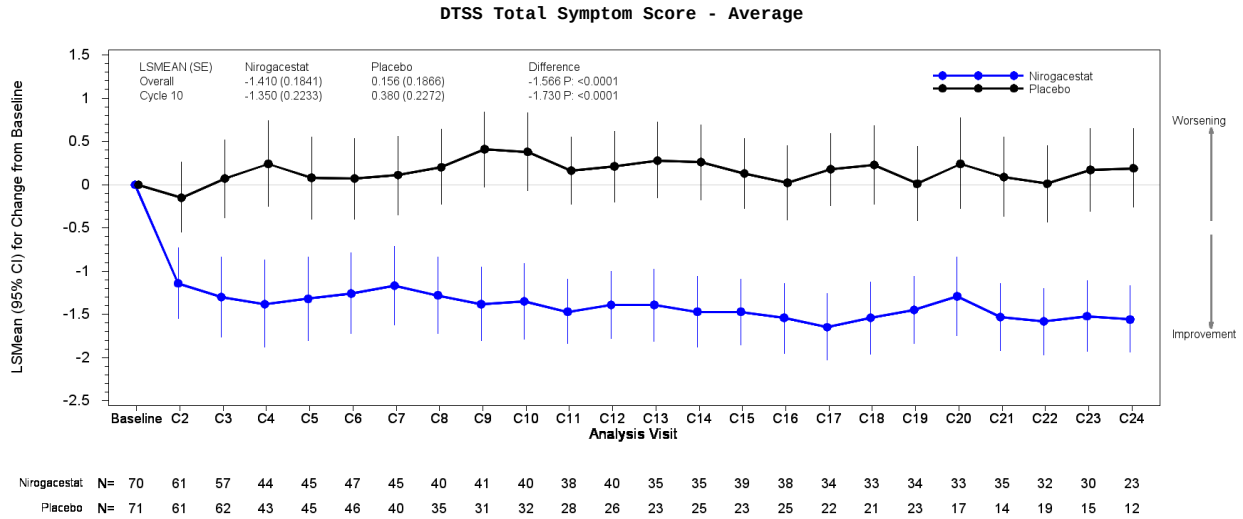


Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.1.1, Dataset(s): ADSL, ADQS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.1.2
Mixed Model Repeated Measures: Change from Baseline in DTSS Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.1.1, Dataset(s): ADSL, ADQS

1.5 PGIC

1.5.1 Table MMRM PGIC

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Effect over Study Duration		
n (%)	68 (97.1)	68 (94.4)
LS Mean [1]	2.944	4.257
LS SE [1]	0.1732	0.1802
95% CI [1]	2.601, 3.287	3.901, 4.613
LS Mean Diff. to Placebo [1]	-1.313	
LS SE Diff. to Placebo [1]	0.2317	
95% CI [1]	-1.771, -0.855	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-0.90 [-1.254, -0.548]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 2		
n (%)	58 (82.9)	51 (70.8)
Mean	3.4	4.0
SD	1.55	1.09
Median	3.0	4.0
Min, Max	1, 7	1, 7
LS Mean [1]	3.396	4.031
LS SE [1]	0.2063	0.2104
95% CI [1]	2.988, 3.805	3.615, 4.447
LS Mean Diff. to Placebo [1]	-0.635	
LS SE Diff. to Placebo [1]	0.2794	
95% CI [1]	-1.188, -0.081	
One-sided p-value [1]	0.0124	
Hedge's G (95% CI)	-0.41 [-0.792, -0.032]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 3		
n (%)	53 (75.7)	59 (81.9)
Mean	3.1	3.9
SD	1.60	1.14
Median	3.0	4.0
Min, Max	1, 7	1, 7
LS Mean [1]	3.273	3.956
LS SE [1]	0.2090	0.2049
95% CI [1]	2.859, 3.686	3.551, 4.362
LS Mean Diff. to Placebo [1]	-0.684	
LS SE Diff. to Placebo [1]	0.2775	
95% CI [1]	-1.233, -0.135	
One-sided p-value [1]	0.0076	
Hedge's G (95% CI)	-0.44 [-0.817, -0.066]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 4		
n (%)	45 (64.3)	35 (48.6)
Mean	3.0	4.3
SD	1.80	1.17
Median	3.0	4.0
Min, Max	1, 6	2, 7
LS Mean [1]	3.350	4.203
LS SE [1]	0.2567	0.2667
95% CI [1]	2.841, 3.859	3.674, 4.731
LS Mean Diff. to Placebo [1]	-0.853	
LS SE Diff. to Placebo [1]	0.3578	
95% CI [1]	-1.562, -0.143	
One-sided p-value [1]	0.0095	
Hedge's G (95% CI)	-0.51 [-0.962, -0.065]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 5		
n (%)	42 (60.0)	41 (56.9)
Mean	3.0	4.0
SD	1.67	1.47
Median	3.0	4.0
Min, Max	1, 6	1, 7
LS Mean [1]	3.272	4.106
LS SE [1]	0.2476	0.2483
95% CI [1]	2.781, 3.762	3.614, 4.598
LS Mean Diff. to Placebo [1]	-0.835	
LS SE Diff. to Placebo [1]	0.3372	
95% CI [1]	-1.503, -0.166	
One-sided p-value [1]	0.0074	
Hedge's G (95% CI)	-0.52 [-0.960, -0.085]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 6		
n (%)	38 (54.3)	35 (48.6)
Mean	3.1	4.2
SD	1.45	1.02
Median	3.0	4.0
Min, Max	1, 6	2, 7
LS Mean [1]	3.138	4.134
LS SE [1]	0.2067	0.2112
95% CI [1]	2.728, 3.548	3.716, 4.552
LS Mean Diff. to Placebo [1]	-0.996	
LS SE Diff. to Placebo [1]	0.2806	
95% CI [1]	-1.552, -0.440	
One-sided p-value [1]	0.0003	
Hedge's G (95% CI)	-0.79 [-1.266, -0.312]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 7		
n (%)	42 (60.0)	35 (48.6)
Mean	2.6	4.1
SD	1.40	1.21
Median	2.0	4.0
Min, Max	1, 6	2, 7
LS Mean [1]	2.998	4.208
LS SE [1]	0.2164	0.2231
95% CI [1]	2.569, 3.426	3.766, 4.650
LS Mean Diff. to Placebo [1]	-1.210	
LS SE Diff. to Placebo [1]	0.2962	
95% CI [1]	-1.798, -0.623	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-0.89 [-1.356, -0.416]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 8		
n (%)	41 (58.6)	29 (40.3)
Mean	3.0	4.4
SD	1.50	1.42
Median	3.0	4.0
Min, Max	1, 6	2, 7
LS Mean [1]	3.177	4.525
LS SE [1]	0.2166	0.2306
95% CI [1]	2.748, 3.606	4.069, 4.982
LS Mean Diff. to Placebo [1]	-1.348	
LS SE Diff. to Placebo [1]	0.3022	
95% CI [1]	-1.947, -0.749	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.01 [-1.518, -0.510]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 9		
n (%)	43 (61.4)	34 (47.2)
Mean	2.7	4.2
SD	1.58	1.35
Median	2.0	4.0
Min, Max	1, 6	2, 7
LS Mean [1]	3.033	4.375
LS SE [1]	0.2141	0.2244
95% CI [1]	2.609, 3.457	3.931, 4.819
LS Mean Diff. to Placebo [1]	-1.342	
LS SE Diff. to Placebo [1]	0.2951	
95% CI [1]	-1.926, -0.757	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-0.98 [-1.460, -0.509]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 10		
n (%)	38 (54.3)	27 (37.5)
Mean	2.6	4.4
SD	1.45	1.39
Median	2.0	4.0
Min, Max	1, 6	2, 7
LS Mean [1]	2.820	4.402
LS SE [1]	0.2175	0.2335
95% CI [1]	2.389, 3.251	3.939, 4.864
LS Mean Diff. to Placebo [1]	-1.582	
LS SE Diff. to Placebo [1]	0.3048	
95% CI [1]	-2.186, -0.978	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.23 [-1.763, -0.690]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 11		
n (%)	34 (48.6)	26 (36.1)
Mean	2.3	4.5
SD	1.38	1.36
Median	2.0	4.0
Min, Max	1, 6	1, 7
LS Mean [1]	2.553	4.261
LS SE [1]	0.2026	0.2167
95% CI [1]	2.152, 2.955	3.832, 4.690
LS Mean Diff. to Placebo [1]	-1.708	
LS SE Diff. to Placebo [1]	0.2806	
95% CI [1]	-2.264, -1.152	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.49 [-2.062, -0.910]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 12		
n (%)	32 (45.7)	24 (33.3)
Mean	2.4	4.1
SD	1.52	1.57
Median	2.0	4.0
Min, Max	1, 6	1, 7
LS Mean [1]	2.869	4.389
LS SE [1]	0.2189	0.2355
95% CI [1]	2.435, 3.302	3.923, 4.855
LS Mean Diff. to Placebo [1]	-1.520	
LS SE Diff. to Placebo [1]	0.3070	
95% CI [1]	-2.129, -0.912	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.26 [-1.842, -0.685]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 13		
n (%)	33 (47.1)	22 (30.6)
Mean	2.6	4.0
SD	1.46	1.90
Median	2.0	4.0
Min, Max	1, 5	1, 7
LS Mean [1]	2.951	4.514
LS SE [1]	0.2270	0.2501
95% CI [1]	2.502, 3.401	4.020, 5.009
LS Mean Diff. to Placebo [1]	-1.563	
LS SE Diff. to Placebo [1]	0.3240	
95% CI [1]	-2.205, -0.922	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.25 [-1.834, -0.659]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 14		
n (%)	33 (47.1)	20 (27.8)
Mean	2.4	4.0
SD	1.41	1.57
Median	2.0	4.0
Min, Max	1, 5	1, 7
LS Mean [1]	2.835	4.348
LS SE [1]	0.2133	0.2404
95% CI [1]	2.412, 3.257	3.873, 4.824
LS Mean Diff. to Placebo [1]	-1.514	
LS SE Diff. to Placebo [1]	0.3075	
95% CI [1]	-2.123, -0.904	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.29 [-1.899, -0.685]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 15		
n (%)	31 (44.3)	23 (31.9)
Mean	2.5	3.9
SD	1.43	1.53
Median	2.0	4.0
Min, Max	1, 6	1, 7
LS Mean [1]	2.844	4.254
LS SE [1]	0.2231	0.2447
95% CI [1]	2.401, 3.286	3.770, 4.739
LS Mean Diff. to Placebo [1]	-1.411	
LS SE Diff. to Placebo [1]	0.3172	
95% CI [1]	-2.040, -0.782	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.16 [-1.745, -0.580]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 16		
n (%)	33 (47.1)	19 (26.4)
Mean	2.5	3.8
SD	1.60	1.72
Median	2.0	4.0
Min, Max	1, 6	1, 7
LS Mean [1]	2.727	4.224
LS SE [1]	0.2277	0.2625
95% CI [1]	2.275, 3.178	3.705, 4.744
LS Mean Diff. to Placebo [1]	-1.498	
LS SE Diff. to Placebo [1]	0.3342	
95% CI [1]	-2.160, -0.836	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.20 [-1.806, -0.587]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 17		
n (%)	31 (44.3)	18 (25.0)
Mean	2.3	3.8
SD	1.35	1.86
Median	2.0	4.0
Min, Max	1, 5	1, 7
LS Mean [1]	2.752	4.093
LS SE [1]	0.2255	0.2614
95% CI [1]	2.305, 3.199	3.576, 4.611
LS Mean Diff. to Placebo [1]	-1.341	
LS SE Diff. to Placebo [1]	0.3323	
95% CI [1]	-2.000, -0.682	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.10 [-1.715, -0.475]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 18		
n (%)	33 (47.1)	20 (27.8)
Mean	2.6	4.4
SD	1.50	1.57
Median	2.0	4.5
Min, Max	1, 7	1, 7
LS Mean [1]	2.903	4.489
LS SE [1]	0.2305	0.2664
95% CI [1]	2.446, 3.360	3.961, 5.016
LS Mean Diff. to Placebo [1]	-1.586	
LS SE Diff. to Placebo [1]	0.3392	
95% CI [1]	-2.259, -0.913	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.24 [-1.847, -0.639]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 19		
n (%)	32 (45.7)	18 (25.0)
Mean	2.7	3.9
SD	1.52	1.80
Median	3.0	4.0
Min, Max	1, 6	1, 7
LS Mean [1]	2.877	4.317
LS SE [1]	0.2184	0.2590
95% CI [1]	2.444, 3.309	3.805, 4.830
LS Mean Diff. to Placebo [1]	-1.440	
LS SE Diff. to Placebo [1]	0.3255	
95% CI [1]	-2.085, -0.796	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.21 [-1.836, -0.587]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 20		
n (%)	29 (41.4)	16 (22.2)
Mean	2.3	4.2
SD	1.42	1.87
Median	2.0	5.0
Min, Max	1, 5	1, 7
LS Mean [1]	2.822	4.563
LS SE [1]	0.2345	0.2834
95% CI [1]	2.358, 3.287	4.002, 5.125
LS Mean Diff. to Placebo [1]	-1.741	
LS SE Diff. to Placebo [1]	0.3555	
95% CI [1]	-2.446, -1.036	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.40 [-2.078, -0.727]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 21		
n (%)	32 (45.7)	14 (19.4)
Mean	2.5	4.0
SD	1.41	1.92
Median	2.0	4.5
Min, Max	1, 5	1, 7
LS Mean [1]	2.847	4.142
LS SE [1]	0.2182	0.2777
95% CI [1]	2.415, 3.279	3.593, 4.692
LS Mean Diff. to Placebo [1]	-1.295	
LS SE Diff. to Placebo [1]	0.3407	
95% CI [1]	-1.970, -0.620	
One-sided p-value [1]	0.0001	
Hedge's G (95% CI)	-1.08 [-1.744, -0.413]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 22		
n (%)	31 (44.3)	18 (25.0)
Mean	2.5	3.3
SD	1.46	1.71
Median	2.0	3.5
Min, Max	1, 6	1, 6
LS Mean [1]	2.722	3.950
LS SE [1]	0.2088	0.2535
95% CI [1]	2.308, 3.135	3.448, 4.452
LS Mean Diff. to Placebo [1]	-1.228	
LS SE Diff. to Placebo [1]	0.3155	
95% CI [1]	-1.853, -0.603	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.07 [-1.686, -0.450]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 23		
n (%)	27 (38.6)	12 (16.7)
Mean	2.5	4.1
SD	1.25	1.98
Median	2.0	4.5
Min, Max	1, 5	1, 7
LS Mean [1]	2.725	4.053
LS SE [1]	0.2190	0.2828
95% CI [1]	2.290, 3.160	3.492, 4.614
LS Mean Diff. to Placebo [1]	-1.328	
LS SE Diff. to Placebo [1]	0.3463	
95% CI [1]	-2.016, -0.640	
One-sided p-value [1]	0.0001	
Hedge's G (95% CI)	-1.19 [-1.919, -0.460]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 24		
n (%)	21 (30.0)	10 (13.9)
Mean	2.5	4.6
SD	1.54	1.51
Median	2.0	5.0
Min, Max	1, 5	1, 6
LS Mean [1]	2.830	4.381
LS SE [1]	0.2419	0.3184
95% CI [1]	2.347, 3.312	3.747, 5.016
LS Mean Diff. to Placebo [1]	-1.552	
LS SE Diff. to Placebo [1]	0.3901	
95% CI [1]	-2.330, -0.773	
One-sided p-value [1]	<0.0001	
Hedge's G (95% CI)	-1.40 [-2.232, -0.572]	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 25		
n (%)	18 (25.7)	5 (6.9)
Mean	3.0	5.2
SD	1.68	0.84
Median	2.5	5.0
Min, Max	1, 7	4, 6
Cycle 26		
n (%)	11 (15.7)	6 (8.3)
Mean	2.8	4.2
SD	1.25	1.47
Median	3.0	4.5
Min, Max	1, 5	2, 6

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 27		
n (%)	12 (17.1)	4 (5.6)
Mean	2.8	3.0
SD	1.47	1.41
Median	3.0	2.5
Min, Max	1, 5	2, 5
Cycle 28		
n (%)	12 (17.1)	2 (2.8)
Mean	2.4	5.5
SD	1.08	0.71
Median	2.0	5.5
Min, Max	1, 5	5, 6

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 29		
n (%)	11 (15.7)	3 (4.2)
Mean	2.7	4.0
SD	1.42	1.00
Median	2.0	4.0
Min, Max	1, 5	3, 5
Cycle 30		
n (%)	8 (11.4)	4 (5.6)
Mean	2.6	3.3
SD	1.77	1.26
Median	2.0	3.0
Min, Max	1, 5	2, 5

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 31		
n (%)	7 (10.0)	4 (5.6)
Mean	2.3	4.5
SD	1.25	1.29
Median	2.0	4.5
Min, Max	1, 5	3, 6
Cycle 32		
n (%)	6 (8.6)	2 (2.8)
Mean	2.7	4.5
SD	1.21	2.12
Median	2.0	4.5
Min, Max	2, 5	3, 6

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 33		
n (%)	5 (7.1)	0
Mean	1.8	
SD	0.84	
Median	2.0	
Min, Max	1, 3	
Cycle 34		
n (%)	1 (1.4)	0
Mean	1.0	
SD	NA	
Median	1.0	
Min, Max	1, 1	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 36		
n (%)	1 (1.4)	0
Mean	1.0	
SD	NA	
Median	1.0	
Min, Max	1, 1	
Cycle 37		
n (%)	1 (1.4)	0
Mean	1.0	
SD	NA	
Median	1.0	
Min, Max	1, 1	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

Table 64.7.1
Summary of Patient Global Impression of Change (PGIC) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Placebo (N=72) Actual Value
Patient Global Impression of Change		
Cycle 40		
n (%)	1 (1.4)	0
Mean	6.0	
SD	NA	
Median	6.0	
Min, Max	6, 6	
Follow-Up		
n (%)	7 (10.0)	1 (1.4)
Mean	4.1	4.0
SD	1.57	NA
Median	5.0	4.0
Min, Max	2, 6	4, 4

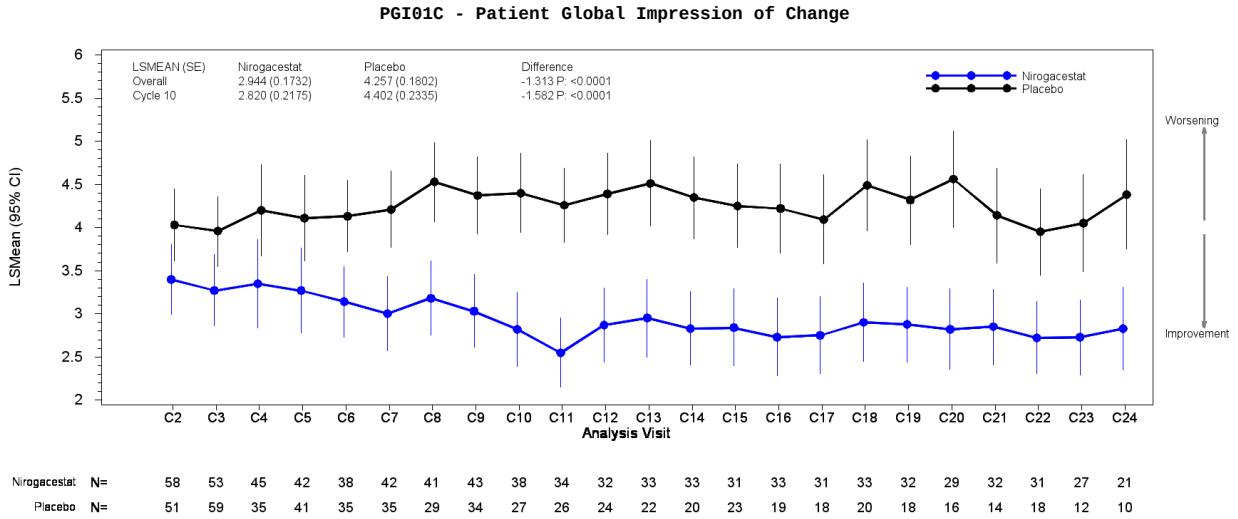
Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A smaller value (<4) indicated improvement of PGIC and a bigger value (>4) indicated worsening of PGIC. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pgic.sas Output Generated: 2025-05-21T12:32 Source: ADSL, ADQS

1.5.2 Figure MMRM PGIC

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.7.2
Mixed Model Repeated Measures: Patient Global Impression of Change (PGIC) by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.7.1, Dataset(s): ADSL, ADQS

Page 1 of 1

1.6 PGIS

1.6.1 Table MMRM PGIS

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Patient Global Impression of Severity				
Baseline [1]				
n (%)	70 (100.0)		70 (97.2)	
Mean	1.8		1.6	
SD	0.89		0.89	
Median	2.0		2.0	
Min, Max	0, 3		0, 3	
Effect over Study Duration				
n (%)		68 (97.1)		67 (93.1)
LS Mean [2]		-0.738		-0.153
LS SE [2]		0.0747		0.0792
95% CI [2]		-0.886, -0.590		-0.310, 0.003
LS Mean Diff. to Placebo [2]		-0.584		
LS SE Diff. to Placebo [2]		0.1009		
95% CI [2]		-0.784, -0.385		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.92 [-1.280, -0.570]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 2				
n (%)	59 (84.3)	59 (84.3)	51 (70.8)	50 (69.4)
Mean	1.2	-0.6	1.3	-0.3
SD	0.86	0.90	0.82	0.66
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 3	-2, 1	0, 3	-2, 1
LS Mean [2]		-0.503		-0.392
LS SE [2]		0.1105		0.1156
95% CI [2]		-0.722, -0.284		-0.621, -0.163
LS Mean Diff. to Placebo [2]		-0.111		
LS SE Diff. to Placebo [2]		0.1547		
95% CI [2]		-0.418, 0.196		
One-sided p-value [2]		0.2376		
Hedge's G (95% CI)		-0.13 [-0.510, 0.244]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	59 (81.9)	59 (81.9)
Mean	1.0	-0.8	1.6	0.0
SD	0.78	0.80	0.89	0.72
Median	1.0	-1.0	2.0	0.0
Min, Max	0, 3	-2, 1	0, 3	-2, 2
LS Mean [2]		-0.704		-0.112
LS SE [2]		0.1014		0.0989
95% CI [2]		-0.904, -0.503		-0.307, 0.084
LS Mean Diff. to Placebo [2]		-0.592		
LS SE Diff. to Placebo [2]		0.1357		
95% CI [2]		-0.861, -0.323		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.79 [-1.175, -0.405]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 4				
n (%)	45 (64.3)	45 (64.3)	36 (50.0)	35 (48.6)
Mean	1.0	-0.6	1.5	-0.1
SD	0.69	0.88	0.84	0.64
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 3	-2, 1	0, 3	-1, 1
LS Mean [2]		-0.625		-0.215
LS SE [2]		0.1097		0.1172
95% CI [2]		-0.843, -0.408		-0.448, 0.017
LS Mean Diff. to Placebo [2]		-0.410		
LS SE Diff. to Placebo [2]		0.1548		
95% CI [2]		-0.718, -0.102		
One-sided p-value [2]		0.0048		
Hedge's G (95% CI)		-0.57 [-1.022, -0.121]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 5				
n (%)	42 (60.0)	42 (60.0)	41 (56.9)	41 (56.9)
Mean	1.1	-0.6	1.5	-0.1
SD	0.63	0.79	0.95	0.82
Median	1.0	-1.0	2.0	0.0
Min, Max	0, 2	-2, 1	0, 3	-2, 2
LS Mean [2]		-0.500		-0.112
LS SE [2]		0.1065		0.1076
95% CI [2]		-0.711, -0.289		-0.325, 0.102
LS Mean Diff. to Placebo [2]		-0.389		
LS SE Diff. to Placebo [2]		0.1458		
95% CI [2]		-0.678, -0.099		
One-sided p-value [2]		0.0045		
Hedge's G (95% CI)		-0.56 [-1.002, -0.125]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 6				
n (%)	38 (54.3)	38 (54.3)	36 (50.0)	35 (48.6)
Mean	1.1	-0.7	1.4	-0.2
SD	0.70	0.98	0.84	0.86
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 3	-3, 1	0, 3	-2, 2
LS Mean [2]		-0.564		-0.239
LS SE [2]		0.1156		0.1189
95% CI [2]		-0.794, -0.335		-0.475, -0.003
LS Mean Diff. to Placebo [2]		-0.326		
LS SE Diff. to Placebo [2]		0.1608		
95% CI [2]		-0.645, -0.006		
One-sided p-value [2]		0.0229		
Hedge's G (95% CI)		-0.46 [-0.925, 0.005]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Patient Global Impression of Severity				
Cycle 7				
n (%)	43 (61.4)	43 (61.4)	35 (48.6)	34 (47.2)
Mean	1.1	-0.7	1.5	-0.1
SD	0.83	0.89	0.89	0.73
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 3	-3, 1	0, 3	-2, 1
LS Mean [2]		-0.558		-0.146
LS SE [2]		0.1089		0.1161
95% CI [2]		-0.774, -0.342		-0.376, 0.084
LS Mean Diff. to Placebo [2]		-0.412		
LS SE Diff. to Placebo [2]		0.1540		
95% CI [2]		-0.718, -0.106		
One-sided p-value [2]		0.0044		
Hedge's G (95% CI)		-0.59 [-1.050, -0.131]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	30 (41.7)	29 (40.3)
Mean	1.1	-0.7	1.6	-0.1
SD	0.80	0.95	0.85	0.84
Median	1.0	-1.0	2.0	0.0
Min, Max	0, 3	-2, 1	0, 3	-3, 1
LS Mean [2]		-0.569		-0.096
LS SE [2]		0.1176		0.1314
95% CI [2]		-0.802, -0.335		-0.356, 0.165
LS Mean Diff. to Placebo [2]		-0.473		
LS SE Diff. to Placebo [2]		0.1712		
95% CI [2]		-0.813, -0.133		
One-sided p-value [2]		0.0035		
Hedge's G (95% CI)		-0.63 [-1.116, -0.152]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Patient Global Impression of Severity				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	34 (47.2)	33 (45.8)
Mean	0.9	-0.8	1.6	0.0
SD	0.73	1.02	0.95	0.79
Median	1.0	-1.0	2.0	0.0
Min, Max	0, 3	-3, 1	0, 3	-2, 2
LS Mean [2]		-0.663		0.003
LS SE [2]		0.1050		0.1144
95% CI [2]		-0.871, -0.455		-0.224, 0.229
LS Mean Diff. to Placebo [2]		-0.665		
LS SE Diff. to Placebo [2]		0.1494		
95% CI [2]		-0.962, -0.369		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-0.98 [-1.456, -0.502]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Patient Global Impression of Severity				
Cycle 10				
n (%)	38 (54.3)	38 (54.3)	27 (37.5)	27 (37.5)
Mean	0.9	-0.8	1.8	0.1
SD	0.78	0.87	0.93	0.72
Median	1.0	-1.0	2.0	0.0
Min, Max	0, 2	-2, 1	0, 3	-1, 2
LS Mean [2]		-0.725		0.021
LS SE [2]		0.1079		0.1200
95% CI [2]		-0.940, -0.511		-0.218, 0.259
LS Mean Diff. to Placebo [2]		-0.746		
LS SE Diff. to Placebo [2]		0.1559		
95% CI [2]		-1.056, -0.436		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.15 [-1.683, -0.620]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 11				
n (%)	34 (48.6)	34 (48.6)	26 (36.1)	26 (36.1)
Mean	0.8	-0.9	1.8	0.2
SD	0.80	1.10	0.90	0.65
Median	1.0	-1.0	2.0	0.0
Min, Max	0, 3	-3, 1	0, 3	-1, 2
LS Mean [2]		-0.788		-0.013
LS SE [2]		0.1191		0.1308
95% CI [2]		-1.025, -0.551		-0.272, 0.247
LS Mean Diff. to Placebo [2]		-0.775		
LS SE Diff. to Placebo [2]		0.1722		
95% CI [2]		-1.118, -0.433		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.14 [-1.685, -0.586]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 12				
n (%)	32 (45.7)	32 (45.7)	24 (33.3)	24 (33.3)
Mean	1.1	-0.8	1.4	-0.1
SD	0.80	1.09	0.88	0.90
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 3	-3, 2	0, 3	-2, 2
LS Mean [2]		-0.594		-0.162
LS SE [2]		0.1320		0.1455
95% CI [2]		-0.857, -0.331		-0.451, 0.128
LS Mean Diff. to Placebo [2]		-0.432		
LS SE Diff. to Placebo [2]		0.1929		
95% CI [2]		-0.817, -0.048		
One-sided p-value [2]		0.0140		
Hedge's G (95% CI)		-0.59 [-1.131, -0.050]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Patient Global Impression of Severity				
Cycle 13				
n (%)	33 (47.1)	33 (47.1)	23 (31.9)	22 (30.6)
Mean	0.8	-0.9	1.4	-0.1
SD	0.81	1.00	0.84	0.83
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 3	-3, 1	0, 3	-2, 2
LS Mean [2]		-0.845		-0.097
LS SE [2]		0.1148		0.1323
95% CI [2]		-1.073, -0.617		-0.359, 0.166
LS Mean Diff. to Placebo [2]		-0.748		
LS SE Diff. to Placebo [2]		0.1704		
95% CI [2]		-1.087, -0.409		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.16 [-1.742, -0.579]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 14				
n (%)	33 (47.1)	33 (47.1)	21 (29.2)	20 (27.8)
Mean	0.8	-0.9	1.6	-0.1
SD	0.76	1.02	0.87	0.76
Median	1.0	-1.0	2.0	0.0
Min, Max	0, 2	-3, 1	0, 3	-2, 1
LS Mean [2]		-0.729		0.032
LS SE [2]		0.1106		0.1309
95% CI [2]		-0.948, -0.509		-0.228, 0.292
LS Mean Diff. to Placebo [2]		-0.761		
LS SE Diff. to Placebo [2]		0.1664		
95% CI [2]		-1.092, -0.430		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.23 [-1.836, -0.630]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Patient Global Impression of Severity				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	22 (30.6)
Mean	0.8	-0.9	1.5	-0.2
SD	0.69	1.03	0.99	0.75
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-3, 1	0, 3	-2, 1
LS Mean [2]		-0.836		-0.089
LS SE [2]		0.1080		0.1229
95% CI [2]		-1.051, -0.622		-0.333, 0.155
LS Mean Diff. to Placebo [2]		-0.747		
LS SE Diff. to Placebo [2]		0.1581		
95% CI [2]		-1.061, -0.433		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.26 [-1.860, -0.666]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 16				
n (%)	32 (45.7)	32 (45.7)	18 (25.0)	18 (25.0)
Mean	0.7	-0.9	1.3	-0.2
SD	0.63	0.88	1.03	0.71
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-3, 0	0, 3	-2, 1
LS Mean [2]		-0.892		-0.044
LS SE [2]		0.0998		0.1227
95% CI [2]		-1.090, -0.694		-0.288, 0.200
LS Mean Diff. to Placebo [2]		-0.848		
LS SE Diff. to Placebo [2]		0.1528		
95% CI [2]		-1.152, -0.544		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.54 [-2.197, -0.892]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 17				
n (%)	31 (44.3)	31 (44.3)	18 (25.0)	18 (25.0)
Mean	0.8	-1.0	1.3	-0.1
SD	0.62	0.84	1.07	0.83
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-2, 1	0, 3	-1, 2
LS Mean [2]		-0.874		-0.221
LS SE [2]		0.1032		0.1265
95% CI [2]		-1.079, -0.669		-0.472, 0.031
LS Mean Diff. to Placebo [2]		-0.653		
LS SE Diff. to Placebo [2]		0.1590		
95% CI [2]		-0.970, -0.337		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.15 [-1.769, -0.522]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 18				
n (%)	33 (47.1)	33 (47.1)	20 (27.8)	19 (26.4)
Mean	0.8	-0.9	1.6	-0.1
SD	0.65	0.97	1.00	0.94
Median	1.0	-1.0	1.5	0.0
Min, Max	0, 2	-3, 1	0, 3	-2, 2
LS Mean [2]		-0.885		-0.156
LS SE [2]		0.1034		0.1266
95% CI [2]		-1.090, -0.679		-0.408, 0.095
LS Mean Diff. to Placebo [2]		-0.728		
LS SE Diff. to Placebo [2]		0.1584		
95% CI [2]		-1.043, -0.413		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.26 [-1.871, -0.643]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 19				
n (%)	32 (45.7)	32 (45.7)	18 (25.0)	17 (23.6)
Mean	0.8	-0.8	1.2	-0.1
SD	0.68	1.03	0.79	0.90
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-3, 1	0, 3	-2, 1
LS Mean [2]		-0.718		-0.125
LS SE [2]		0.1131		0.1477
95% CI [2]		-0.943, -0.492		-0.419, 0.169
LS Mean Diff. to Placebo [2]		-0.593		
LS SE Diff. to Placebo [2]		0.1810		
95% CI [2]		-0.953, -0.232		
One-sided p-value [2]		0.0008		
Hedge's G (95% CI)		-0.93 [-1.542, -0.310]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 20				
n (%)	29 (41.4)	29 (41.4)	16 (22.2)	16 (22.2)
Mean	0.8	-1.1	1.4	0.0
SD	0.62	1.01	0.96	0.73
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-3, 1	0, 3	-1, 1
LS Mean [2]		-0.875		-0.221
LS SE [2]		0.1049		0.1330
95% CI [2]		-1.084, -0.666		-0.485, 0.044
LS Mean Diff. to Placebo [2]		-0.654		
LS SE Diff. to Placebo [2]		0.1663		
95% CI [2]		-0.986, -0.323		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		-1.16 [-1.817, -0.505]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	14 (19.4)	14 (19.4)
Mean	0.8	-1.0	1.4	0.0
SD	0.61	0.93	0.84	0.78
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-3, 1	0, 3	-1, 1
LS Mean [2]		-0.913		-0.296
LS SE [2]		0.0966		0.1322
95% CI [2]		-1.105, -0.720		-0.558, -0.033
LS Mean Diff. to Placebo [2]		-0.617		
LS SE Diff. to Placebo [2]		0.1598		
95% CI [2]		-0.935, -0.299		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		-1.14 [-1.810, -0.471]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score / Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	19 (26.4)	19 (26.4)
Mean	0.8	-0.9	1.3	-0.2
SD	0.65	0.89	0.87	0.76
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-2, 1	0, 3	-2, 1
LS Mean [2]		-0.853		-0.298
LS SE [2]		0.0958		0.1204
95% CI [2]		-1.043, -0.662		-0.538, -0.059
LS Mean Diff. to Placebo [2]		-0.554		
LS SE Diff. to Placebo [2]		0.1493		
95% CI [2]		-0.851, -0.257		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		-1.05 [-1.652, -0.438]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 23				
n (%)	28 (40.0)	28 (40.0)	12 (16.7)	12 (16.7)
Mean	0.9	-0.8	1.6	0.0
SD	0.66	0.92	0.79	0.95
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-2, 1	1, 3	-1, 2
LS Mean [2]		-0.788		-0.225
LS SE [2]		0.1051		0.1466
95% CI [2]		-0.997, -0.578		-0.517, 0.067
LS Mean Diff. to Placebo [2]		-0.563		
LS SE Diff. to Placebo [2]		0.1763		
95% CI [2]		-0.915, -0.211		
One-sided p-value [2]		0.0011		
Hedge's G (95% CI)		-1.02 [-1.729, -0.305]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 24				
n (%)	21 (30.0)	21 (30.0)	11 (15.3)	11 (15.3)
Mean	0.6	-1.2	1.2	-0.1
SD	0.74	0.83	0.87	0.70
Median	0.0	-1.0	1.0	0.0
Min, Max	0, 2	-3, 0	0, 3	-1, 1
LS Mean [2]		-0.975		-0.329
LS SE [2]		0.1087		0.1453
95% CI [2]		-1.193, -0.757		-0.621, -0.038
LS Mean Diff. to Placebo [2]		-0.646		
LS SE Diff. to Placebo [2]		0.1799		
95% CI [2]		-1.007, -0.284		
One-sided p-value [2]		0.0004		
Hedge's G (95% CI)		-1.28 [-2.071, -0.484]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
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[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	0.7	-1.0	1.8	0.0
SD	0.67	0.88	1.10	0.00
Median	1.0	-1.0	1.0	0.0
Min, Max	0, 2	-2, 0	1, 3	0, 0
Cycle 26				
n (%)	11 (15.7)	11 (15.7)	6 (8.3)	6 (8.3)
Mean	0.6	-1.2	1.8	-0.2
SD	0.50	0.75	0.98	0.75
Median	1.0	-1.0	1.5	0.0
Min, Max	0, 1	-2, 0	1, 3	-1, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	0.8	-1.1	2.0	0.3
SD	0.62	1.00	0.82	0.96
Median	1.0	-1.0	2.0	0.5
Min, Max	0, 2	-3, 0	1, 3	-1, 1
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	2 (2.8)	2 (2.8)
Mean	0.8	-1.0	2.0	0.0
SD	0.72	1.13	1.41	0.00
Median	1.0	-1.0	2.0	0.0
Min, Max	0, 2	-3, 1	1, 3	0, 0

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CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 29				
n (%)	11 (15.7)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	0.7	-1.3	1.7	-0.3
SD	0.65	1.01	0.58	1.15
Median	1.0	-1.0	2.0	-1.0
Min, Max	0, 2	-3, 0	1, 2	-1, 1
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	0.6	-1.5	1.5	-0.5
SD	0.74	1.20	1.29	0.58
Median	0.5	-2.0	1.5	-0.5
Min, Max	0, 2	-3, 1	0, 3	-1, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Patient Global Impression of Severity				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	4 (5.6)	4 (5.6)
Mean	1.0	-1.0	1.8	0.0
SD	0.00	1.00	0.96	0.00
Median	1.0	-1.0	1.5	0.0
Min, Max	1, 1	-2, 0	1, 3	0, 0
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	0.7	-1.3	2.0	1.0
SD	0.52	1.21	0.00	0.00
Median	1.0	-1.5	2.0	1.0
Min, Max	0, 1	-3, 0	2, 2	1, 1

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	0.6	-1.6		
SD	0.55	1.14		
Median	1.0	-2.0		
Min, Max	0, 1	-3, 0		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-2.0		
SD	NA	NA		
Median	0.0	-2.0		
Min, Max	0, 0	-2, -2		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-1.0		
SD	NA	NA		
Median	0.0	-1.0		
Min, Max	0, 0	-1, -1		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	0.0	-1.0		
SD	NA	NA		
Median	0.0	-1.0		
Min, Max	0, 0	-1, -1		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
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Table 64.6.1
Summary and Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double-Blind Phase
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Patient Global Impression of Severity				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	1.0	1.0		
SD	NA	NA		
Median	1.0	1.0		
Min, Max	1, 1	1, 1		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	1.3	-0.4	0.0	-1.0
SD	0.76	0.53	NA	NA
Median	1.0	0.0	0.0	-1.0
Min, Max	0, 2	-1, 0	0, 0	-1, -1

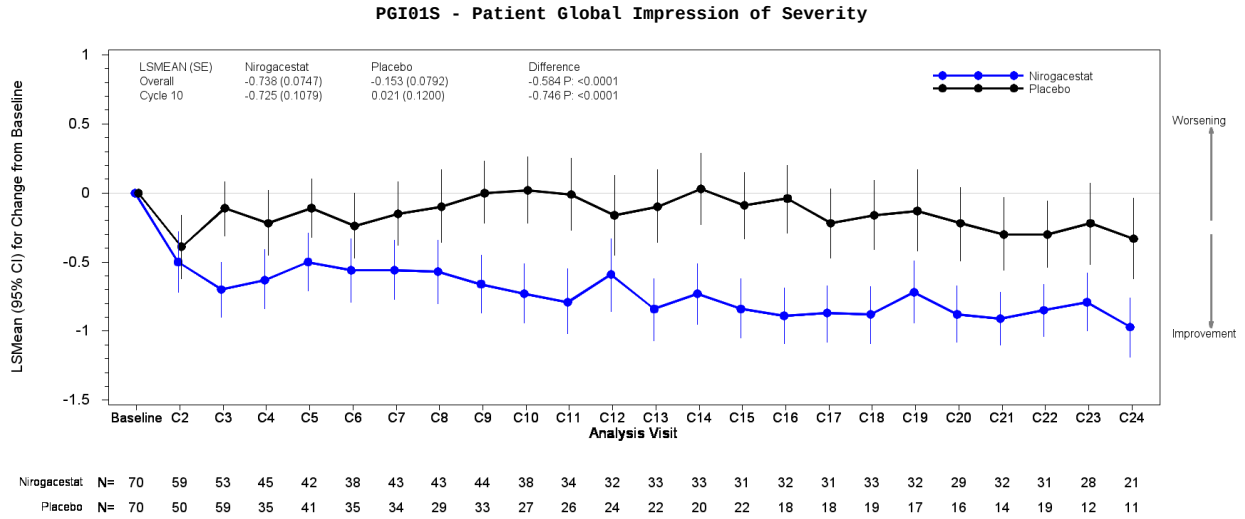
Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; SE = Standard error
Note: A positive change from Baseline value indicated worsening of PGIS and a negative change from Baseline value indicated improvement of PGIS. A negative LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PGIS score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation. Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

1.6.2 Figure MMRM PGIS

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.6.2
Mixed Model Repeated Measures: Change from Baseline in Patient Global Impression of Severity (PGIS) by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.6.1, Dataset(s): ADSL, ADQS

1.7 PROMIS PF

1.7.1 Table MMRM PROMIS PF

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
PF10a T-Score				
Baseline [1]				
n (%)	70 (100.0)		71 (98.6)	
Mean	44.2		44.3	
SD	8.79		9.56	
Median	42.6		42.6	
Min, Max	26, 62		24, 62	
Effect over Study Duration				
n (%)		68 (97.1)		70 (97.2)
LS Mean [2]		4.877		0.438
LS SE [2]		0.5620		0.6156
95% CI [2]		3.768, 5.987		-0.776, 1.653
LS Mean Diff. to Placebo [2]		4.439		
LS SE Diff. to Placebo [2]		0.7773		
95% CI [2]		2.905, 5.973		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.91 [0.555, 1.256]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 2				
n (%)	61 (87.1)	61 (87.1)	55 (76.4)	55 (76.4)
Mean	46.3	2.0	45.2	-0.5
SD	10.12	4.34	8.59	4.62
Median	44.4	1.6	44.4	0.0
Min, Max	23, 62	-10, 16	30, 62	-11, 18
LS Mean [2]		1.684		-0.620
LS SE [2]		0.7935		0.7981
95% CI [2]		0.113, 3.254		-2.200, 0.959
LS Mean Diff. to Placebo [2]		2.304		
LS SE Diff. to Placebo [2]		1.0848		
95% CI [2]		0.156, 4.452		
One-sided p-value [2]		0.0179		
Hedge's G (95% CI)		0.38 [0.012, 0.747]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 3				
n (%)	53 (75.7)	53 (75.7)	62 (86.1)	62 (86.1)
Mean	48.4	3.7	43.9	-0.5
SD	9.32	5.54	8.77	4.64
Median	47.9	3.8	43.5	0.0
Min, Max	24, 62	-11, 15	27, 62	-15, 10
LS Mean [2]		2.953		-0.803
LS SE [2]		0.8901		0.8672
95% CI [2]		1.193, 4.712		-2.517, 0.912
LS Mean Diff. to Placebo [2]		3.756		
LS SE Diff. to Placebo [2]		1.2048		
95% CI [2]		1.372, 6.139		
One-sided p-value [2]		0.0011		
Hedge's G (95% CI)		0.56 [0.189, 0.937]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 4				
n (%)	46 (65.7)	46 (65.7)	38 (52.8)	38 (52.8)
Mean	50.4	4.2	45.7	0.1
SD	8.18	5.83	9.54	4.89
Median	50.3	4.3	43.1	0.0
Min, Max	27, 62	-9, 16	33, 62	-14, 14
LS Mean [2]		3.662		0.386
LS SE [2]		0.9536		0.9610
95% CI [2]		1.774, 5.549		-1.516, 2.288
LS Mean Diff. to Placebo [2]		3.276		
LS SE Diff. to Placebo [2]		1.3172		
95% CI [2]		0.667, 5.885		
One-sided p-value [2]		0.0072		
Hedge's G (95% CI)		0.53 [0.089, 0.963]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
PF10a T-Score				
Cycle 5				
n (%)	44 (62.9)	44 (62.9)	43 (59.7)	42 (58.3)
Mean	49.3	4.6	46.9	1.3
SD	8.81	5.68	9.48	5.10
Median	50.3	3.6	45.5	1.9
Min, Max	26, 62	-4, 18	30, 62	-14, 11
LS Mean [2]		3.533		0.652
LS SE [2]		0.8680		0.8703
95% CI [2]		1.817, 5.249		-1.069, 2.373
LS Mean Diff. to Placebo [2]		2.881		
LS SE Diff. to Placebo [2]		1.1885		
95% CI [2]		0.530, 5.232		
One-sided p-value [2]		0.0084		
Hedge's G (95% CI)		0.51 [0.076, 0.935]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 6				
n (%)	39 (55.7)	39 (55.7)	36 (50.0)	36 (50.0)
Mean	49.4	4.0	46.1	0.5
SD	9.21	5.48	8.80	4.07
Median	49.4	2.7	46.1	0.0
Min, Max	24, 62	-6, 18	29, 62	-9, 9
LS Mean [2]		3.675		-0.006
LS SE [2]		0.7538		0.7663
95% CI [2]		2.185, 5.166		-1.520, 1.509
LS Mean Diff. to Placebo [2]		3.681		
LS SE Diff. to Placebo [2]		1.0288		
95% CI [2]		1.646, 5.716		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		0.79 [0.320, 1.261]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 7				
n (%)	44 (62.9)	44 (62.9)	38 (52.8)	38 (52.8)
Mean	49.4	4.7	46.3	0.2
SD	9.75	6.39	9.86	4.59
Median	51.2	3.9	45.0	0.0
Min, Max	28, 62	-9, 21	30, 62	-8, 12
LS Mean [2]		3.943		0.298
LS SE [2]		0.8081		0.8320
95% CI [2]		2.346, 5.540		-1.346, 1.941
LS Mean Diff. to Placebo [2]		3.645		
LS SE Diff. to Placebo [2]		1.1166		
95% CI [2]		1.438, 5.852		
One-sided p-value [2]		0.0007		
Hedge's G (95% CI)		0.69 [0.247, 1.141]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 8				
n (%)	43 (61.4)	43 (61.4)	31 (43.1)	31 (43.1)
Mean	49.0	4.7	42.9	-0.5
SD	9.79	6.71	8.73	3.51
Median	49.4	2.7	41.7	0.0
Min, Max	27, 62	-11, 21	29, 62	-9, 5
LS Mean [2]		4.776		-0.736
LS SE [2]		0.7878		0.8300
95% CI [2]		3.220, 6.332		-2.375, 0.904
LS Mean Diff. to Placebo [2]		5.512		
LS SE Diff. to Placebo [2]		1.1015		
95% CI [2]		3.335, 7.688		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.11 [0.619, 1.610]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 9				
n (%)	44 (62.9)	44 (62.9)	35 (48.6)	35 (48.6)
Mean	50.7	5.9	44.3	-0.7
SD	9.19	6.69	10.27	5.04
Median	52.3	5.4	41.7	0.0
Min, Max	29, 62	-11, 21	25, 62	-15, 11
LS Mean [2]		5.032		-0.570
LS SE [2]		0.8044		0.8487
95% CI [2]		3.443, 6.620		-2.246, 1.105
LS Mean Diff. to Placebo [2]		5.602		
LS SE Diff. to Placebo [2]		1.1265		
95% CI [2]		3.377, 7.827		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.08 [0.603, 1.552]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 10				
n (%)	39 (55.7)	39 (55.7)	28 (38.9)	28 (38.9)
Mean	51.5	6.2	43.1	-1.0
SD	9.14	6.49	10.00	4.73
Median	53.4	4.9	42.6	0.0
Min, Max	29, 62	-9, 19	29, 62	-13, 6
LS Mean [2]		5.644		-0.581
LS SE [2]		0.7837		0.8452
95% CI [2]		4.096, 7.193		-2.250, 1.088
LS Mean Diff. to Placebo [2]		6.225		
LS SE Diff. to Placebo [2]		1.1092		
95% CI [2]		4.033, 8.417		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.32 [0.784, 1.852]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 11				
n (%)	35 (50.0)	35 (50.0)	26 (36.1)	26 (36.1)
Mean	50.8	6.1	43.2	-0.5
SD	9.54	7.54	8.50	4.10
Median	51.2	6.1	43.1	0.0
Min, Max	27, 62	-11, 24	31, 62	-11, 6
LS Mean [2]		5.817		-0.636
LS SE [2]		0.8127		0.8880
95% CI [2]		4.211, 7.422		-2.390, 1.117
LS Mean Diff. to Placebo [2]		6.453		
LS SE Diff. to Placebo [2]		1.1615		
95% CI [2]		4.157, 8.749		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.38 [0.812, 1.939]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 12				
n (%)	36 (51.4)	36 (51.4)	24 (33.3)	24 (33.3)
Mean	50.3	6.7	45.7	0.6
SD	10.53	8.10	9.40	5.24
Median	51.2	6.3	46.1	0.8
Min, Max	26, 62	-14, 24	27, 62	-12, 13
LS Mean [2]		5.500		-0.364
LS SE [2]		0.9043		1.0097
95% CI [2]		3.714, 7.287		-2.358, 1.630
LS Mean Diff. to Placebo [2]		5.864		
LS SE Diff. to Placebo [2]		1.3189		
95% CI [2]		3.258, 8.471		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.12 [0.565, 1.673]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 13				
n (%)	35 (50.0)	35 (50.0)	23 (31.9)	23 (31.9)
Mean	50.0	5.1	43.4	-0.7
SD	10.46	7.26	10.32	6.59
Median	49.4	3.8	43.5	0.0
Min, Max	27, 62	-6, 21	28, 62	-17, 11
LS Mean [2]		5.082		-1.050
LS SE [2]		0.9099		1.0314
95% CI [2]		3.284, 6.881		-3.087, 0.987
LS Mean Diff. to Placebo [2]		6.132		
LS SE Diff. to Placebo [2]		1.3396		
95% CI [2]		3.484, 8.780		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.18 [0.608, 1.744]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 14				
n (%)	34 (48.6)	34 (48.6)	22 (30.6)	22 (30.6)
Mean	51.8	6.3	44.8	1.2
SD	10.03	7.89	10.74	4.58
Median	53.4	4.6	43.1	0.0
Min, Max	27, 62	-9, 24	27, 62	-12, 11
LS Mean [2]		5.283		-0.369
LS SE [2]		0.8876		1.0161
95% CI [2]		3.529, 7.038		-2.376, 1.639
LS Mean Diff. to Placebo [2]		5.652		
LS SE Diff. to Placebo [2]		1.3146		
95% CI [2]		3.053, 8.251		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.13 [0.550, 1.701]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 15				
n (%)	31 (44.3)	31 (44.3)	23 (31.9)	23 (31.9)
Mean	49.6	6.0	45.5	1.8
SD	10.02	7.69	10.12	4.87
Median	51.2	4.3	45.5	0.0
Min, Max	32, 62	-11, 21	31, 62	-6, 14
LS Mean [2]		5.252		1.026
LS SE [2]		0.8639		0.9815
95% CI [2]		3.545, 6.960		-0.913, 2.966
LS Mean Diff. to Placebo [2]		4.226		
LS SE Diff. to Placebo [2]		1.2713		
95% CI [2]		1.712, 6.739		
One-sided p-value [2]		0.0006		
Hedge's G (95% CI)		0.89 [0.322, 1.451]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
PF10a T-Score				
Cycle 16				
n (%)	35 (50.0)	35 (50.0)	21 (29.2)	21 (29.2)
Mean	50.5	5.6	46.0	1.5
SD	9.28	7.01	10.13	4.09
Median	49.4	5.9	45.5	0.0
Min, Max	30, 62	-11, 21	30, 62	-6, 11
LS Mean [2]		5.117		0.902
LS SE [2]		0.8285		0.9649
95% CI [2]		3.479, 6.756		-1.006, 2.809
LS Mean Diff. to Placebo [2]		4.216		
LS SE Diff. to Placebo [2]		1.2374		
95% CI [2]		1.768, 6.663		
One-sided p-value [2]		0.0004		
Hedge's G (95% CI)		0.89 [0.326, 1.457]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 17				
n (%)	32 (45.7)	32 (45.7)	21 (29.2)	21 (29.2)
Mean	49.8	5.7	47.9	0.8
SD	10.23	7.75	10.01	5.76
Median	50.3	5.8	46.6	0.0
Min, Max	28, 62	-15, 24	32, 62	-12, 12
LS Mean [2]		5.520		1.154
LS SE [2]		0.9458		1.1052
95% CI [2]		3.649, 7.390		-1.031, 3.339
LS Mean Diff. to Placebo [2]		4.366		
LS SE Diff. to Placebo [2]		1.4248		
95% CI [2]		1.547, 7.184		
One-sided p-value [2]		0.0013		
Hedge's G (95% CI)		0.83 [0.260, 1.406]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 18				
n (%)	35 (50.0)	35 (50.0)	21 (29.2)	21 (29.2)
Mean	50.5	6.2	46.2	0.0
SD	10.22	7.44	10.13	5.21
Median	51.2	4.3	44.4	0.0
Min, Max	28, 62	-9, 21	32, 62	-11, 11
LS Mean [2]		5.873		0.845
LS SE [2]		0.9303		1.1067
95% CI [2]		4.034, 7.713		-1.342, 3.033
LS Mean Diff. to Placebo [2]		5.028		
LS SE Diff. to Placebo [2]		1.4156		
95% CI [2]		2.228, 7.828		
One-sided p-value [2]		0.0003		
Hedge's G (95% CI)		0.94 [0.372, 1.509]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
PF10a T-Score				
Cycle 19				
n (%)	34 (48.6)	34 (48.6)	21 (29.2)	21 (29.2)
Mean	51.4	6.6	47.0	1.5
SD	8.29	7.43	8.80	6.09
Median	51.2	5.5	46.6	0.0
Min, Max	36, 62	-9, 24	33, 62	-12, 19
LS Mean [2]		5.687		1.310
LS SE [2]		0.8648		1.0501
95% CI [2]		3.977, 7.397		-0.765, 3.386
LS Mean Diff. to Placebo [2]		4.377		
LS SE Diff. to Placebo [2]		1.3282		
95% CI [2]		1.750, 7.003		
One-sided p-value [2]		0.0006		
Hedge's G (95% CI)		0.88 [0.314, 1.451]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 20				
n (%)	30 (42.9)	30 (42.9)	16 (22.2)	16 (22.2)
Mean	49.3	5.5	47.1	2.4
SD	9.43	7.38	9.36	7.52
Median	48.7	5.0	46.1	1.1
Min, Max	29, 62	-14, 20	30, 62	-6, 27
LS Mean [2]		4.518		1.966
LS SE [2]		0.9592		1.2199
95% CI [2]		2.620, 6.415		-0.447, 4.378
LS Mean Diff. to Placebo [2]		2.552		
LS SE Diff. to Placebo [2]		1.5245		
95% CI [2]		-0.464, 5.569		
One-sided p-value [2]		0.0483		
Hedge's G (95% CI)		0.49 [-0.126, 1.104]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 21				
n (%)	32 (45.7)	32 (45.7)	15 (20.8)	15 (20.8)
Mean	50.7	6.8	46.0	2.0
SD	9.64	7.00	8.70	7.52
Median	50.3	6.4	44.4	0.0
Min, Max	33, 62	-4, 24	34, 62	-4, 27
LS Mean [2]		5.566		1.526
LS SE [2]		0.9202		1.2134
95% CI [2]		3.746, 7.387		-0.874, 3.925
LS Mean Diff. to Placebo [2]		4.041		
LS SE Diff. to Placebo [2]		1.4958		
95% CI [2]		1.081, 7.001		
One-sided p-value [2]		0.0039		
Hedge's G (95% CI)		0.79 [0.153, 1.420]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 22				
n (%)	31 (44.3)	31 (44.3)	20 (27.8)	20 (27.8)
Mean	50.5	6.1	47.9	3.0
SD	9.88	8.31	8.76	6.95
Median	49.4	6.2	46.6	0.6
Min, Max	32, 62	-18, 24	32, 62	-6, 27
LS Mean [2]		5.451		2.328
LS SE [2]		0.9122		1.1756
95% CI [2]		3.647, 7.255		0.003, 4.652
LS Mean Diff. to Placebo [2]		3.123		
LS SE Diff. to Placebo [2]		1.4628		
95% CI [2]		0.230, 6.017		
One-sided p-value [2]		0.0173		
Hedge's G (95% CI)		0.61 [0.032, 1.181]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 23				
n (%)	29 (41.4)	29 (41.4)	14 (19.4)	14 (19.4)
Mean	49.1	5.0	46.3	2.1
SD	9.70	6.89	9.30	8.07
Median	49.4	4.6	46.1	0.0
Min, Max	32, 62	-9, 20	31, 62	-8, 27
LS Mean [2]		5.636		1.928
LS SE [2]		0.9397		1.2652
95% CI [2]		3.775, 7.498		-0.578, 4.434
LS Mean Diff. to Placebo [2]		3.709		
LS SE Diff. to Placebo [2]		1.5522		
95% CI [2]		0.633, 6.785		
One-sided p-value [2]		0.0093		
Hedge's G (95% CI)		0.73 [0.078, 1.391]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 24				
n (%)	22 (31.4)	22 (31.4)	11 (15.3)	11 (15.3)
Mean	53.8	8.9	45.3	1.2
SD	9.36	7.21	10.60	9.25
Median	57.7	7.4	46.6	-0.8
Min, Max	36, 62	-2, 24	28, 62	-6, 27
LS Mean [2]		6.971		1.500
LS SE [2]		1.0346		1.4235
95% CI [2]		4.911, 9.031		-1.334, 4.335
LS Mean Diff. to Placebo [2]		5.471		
LS SE Diff. to Placebo [2]		1.7409		
95% CI [2]		2.003, 8.939		
One-sided p-value [2]		0.0012		
Hedge's G (95% CI)		1.11 [0.338, 1.881]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 25				
n (%)	19 (27.1)	19 (27.1)	5 (6.9)	5 (6.9)
Mean	53.9	7.1	38.0	-2.4
SD	8.89	8.31	8.22	3.34
Median	55.8	5.9	37.0	-2.4
Min, Max	36, 62	-9, 24	27, 47	-6, 2
Cycle 26				
n (%)	12 (17.1)	12 (17.1)	6 (8.3)	6 (8.3)
Mean	52.1	4.5	42.9	1.4
SD	8.24	9.55	10.87	3.87
Median	51.2	4.9	41.8	2.2
Min, Max	36, 62	-15, 24	28, 56	-6, 5

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 27				
n (%)	12 (17.1)	12 (17.1)	4 (5.6)	4 (5.6)
Mean	49.4	3.6	42.4	1.7
SD	9.77	7.59	9.86	3.35
Median	46.6	5.1	41.4	1.1
Min, Max	30, 62	-15, 15	33, 53	-2, 6
Cycle 28				
n (%)	12 (17.1)	12 (17.1)	3 (4.2)	3 (4.2)
Mean	50.9	5.1	43.9	-1.8
SD	9.65	8.57	8.90	2.46
Median	51.2	4.6	46.6	-0.8
Min, Max	36, 62	-11, 20	34, 51	-5, 0

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 29				
n (%)	12 (17.1)	12 (17.1)	3 (4.2)	3 (4.2)
Mean	47.3	4.3	42.2	-0.4
SD	8.02	8.34	5.77	4.84
Median	46.1	5.1	45.5	0.7
Min, Max	37, 62	-13, 20	36, 46	-6, 4
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	47.9	8.1	41.9	3.9
SD	7.71	6.30	7.43	6.84
Median	48.0	5.8	45.1	3.4
Min, Max	36, 62	1, 20	31, 47	-4, 13

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	5 (6.9)	5 (6.9)
Mean	49.9	4.6	44.5	1.9
SD	7.14	7.47	6.76	6.40
Median	51.2	6.2	45.5	0.0
Min, Max	39, 62	-9, 15	33, 51	-6, 10
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	46.7	4.8	48.0	-3.2
SD	5.39	7.80	1.98	1.98
Median	46.7	6.2	48.0	-3.2
Min, Max	39, 53	-9, 15	47, 49	-5, -2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	50.3	7.9		
SD	9.05	10.88		
Median	51.2	6.8		
Min, Max	37, 62	-9, 20		
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	61.9	20.2		
SD	NA	NA		
Median	61.9	20.2		
Min, Max	62, 62	20, 20		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	61.9	15.3		
SD	NA	NA		
Median	61.9	15.3		
Min, Max	62, 62	15, 15		
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	61.9	15.3		
SD	NA	NA		
Median	61.9	15.3		
Min, Max	62, 62	15, 15		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF10a T-Score				
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	38.5	4.5		
SD	NA	NA		
Median	38.5	4.5		
Min, Max	39, 39	5, 5		
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	1 (1.4)
Mean	49.1	4.1	45.5	-2.4
SD	11.15	4.73	NA	NA
Median	47.9	2.4	45.5	-2.4
Min, Max	33, 62	-2, 11	46, 46	-2, -2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Baseline [1]				
n (%)	64 (91.4)		68 (94.4)	
Mean	51.8		51.0	
SD	10.45		10.96	
Median	53.0		52.5	
Min, Max	25, 65		21, 65	

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
PF13 Score				
Effect over Study Duration				
n (%)		62 (88.6)		67 (93.1)
LS Mean [2]		4.095		0.040
LS SE [2]		0.6469		0.6451
95% CI [2]		2.816, 5.375		-1.235, 1.315
LS Mean Diff. to Placebo [2]		4.055		
LS SE Diff. to Placebo [2]		0.8440		
95% CI [2]		2.386, 5.724		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.78 [0.423, 1.139]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 2				
n (%)	56 (80.0)	55 (78.6)	53 (73.6)	52 (72.2)
Mean	53.5	1.5	52.5	-0.1
SD	10.78	4.63	9.71	4.79
Median	56.5	2.0	54.0	0.0
Min, Max	23, 65	-12, 10	28, 65	-16, 14
LS Mean [2]		1.394		-0.198
LS SE [2]		0.7779		0.7569
95% CI [2]		-0.146, 2.935		-1.697, 1.301
LS Mean Diff. to Placebo [2]		1.592		
LS SE Diff. to Placebo [2]		1.0287		
95% CI [2]		-0.447, 3.631		
One-sided p-value [2]		0.0623		
Hedge's G (95% CI)		0.28 [-0.098, 0.664]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 3				
n (%)	49 (70.0)	48 (68.6)	60 (83.3)	59 (81.9)
Mean	55.9	3.3	50.6	-0.5
SD	10.09	4.85	10.02	5.54
Median	58.0	2.5	51.5	0.0
Min, Max	24, 65	-4, 15	25, 65	-16, 12
LS Mean [2]		3.027		-0.728
LS SE [2]		0.7697		0.7240
95% CI [2]		1.505, 4.550		-2.161, 0.705
LS Mean Diff. to Placebo [2]		3.755		
LS SE Diff. to Placebo [2]		0.9984		
95% CI [2]		1.779, 5.732		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		0.69 [0.296, 1.080]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 4				
n (%)	44 (62.9)	42 (60.0)	37 (51.4)	35 (48.6)
Mean	58.0	3.7	52.2	-0.3
SD	8.37	4.85	9.71	4.61
Median	60.5	3.0	52.0	-1.0
Min, Max	24, 65	-7, 16	33, 65	-9, 11
LS Mean [2]		3.920		0.250
LS SE [2]		0.7898		0.7780
95% CI [2]		2.355, 5.486		-1.291, 1.792
LS Mean Diff. to Placebo [2]		3.670		
LS SE Diff. to Placebo [2]		1.0514		
95% CI [2]		1.584, 5.756		
One-sided p-value [2]		0.0004		
Hedge's G (95% CI)		0.75 [0.286, 1.214]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 5				
n (%)	42 (60.0)	40 (57.1)	43 (59.7)	40 (55.6)
Mean	56.6	4.2	54.0	1.4
SD	9.45	5.45	10.08	6.00
Median	59.0	2.5	57.0	1.0
Min, Max	22, 65	-4, 17	30, 65	-15, 14
LS Mean [2]		3.285		0.873
LS SE [2]		0.8228		0.7981
95% CI [2]		1.656, 4.913		-0.706, 2.453
LS Mean Diff. to Placebo [2]		2.411		
LS SE Diff. to Placebo [2]		1.0908		
95% CI [2]		0.251, 4.572		
One-sided p-value [2]		0.0145		
Hedge's G (95% CI)		0.47 [0.026, 0.915]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
PF13 Score				
Cycle 6				
n (%)	39 (55.7)	35 (50.0)	36 (50.0)	35 (48.6)
Mean	56.9	3.5	53.3	0.3
SD	9.55	5.13	10.47	4.88
Median	60.0	2.0	55.5	0.0
Min, Max	20, 65	-5, 20	28, 65	-16, 12
LS Mean [2]		3.273		0.420
LS SE [2]		0.7398		0.7211
95% CI [2]		1.809, 4.737		-1.007, 1.846
LS Mean Diff. to Placebo [2]		2.853		
LS SE Diff. to Placebo [2]		0.9713		
95% CI [2]		0.930, 4.777		
One-sided p-value [2]		0.0020		
Hedge's G (95% CI)		0.66 [0.179, 1.141]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 7				
n (%)	44 (62.9)	41 (58.6)	38 (52.8)	36 (50.0)
Mean	56.0	4.2	53.3	-0.1
SD	10.58	5.95	10.50	5.78
Median	61.0	3.0	56.5	0.0
Min, Max	24, 65	-6, 20	31, 65	-14, 15
LS Mean [2]		3.482		0.677
LS SE [2]		0.8356		0.8299
95% CI [2]		1.828, 5.137		-0.965, 2.319
LS Mean Diff. to Placebo [2]		2.806		
LS SE Diff. to Placebo [2]		1.1241		
95% CI [2]		0.579, 5.032		
One-sided p-value [2]		0.0070		
Hedge's G (95% CI)		0.54 [0.086, 0.997]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 8				
n (%)	43 (61.4)	38 (54.3)	31 (43.1)	30 (41.7)
Mean	55.7	3.9	49.6	-1.0
SD	10.36	5.87	11.22	4.76
Median	60.0	2.5	52.0	0.0
Min, Max	23, 65	-6, 19	28, 65	-16, 5
LS Mean [2]		3.789		-0.452
LS SE [2]		0.7704		0.7796
95% CI [2]		2.263, 5.314		-1.995, 1.090
LS Mean Diff. to Placebo [2]		4.241		
LS SE Diff. to Placebo [2]		1.0390		
95% CI [2]		2.183, 6.299		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		0.93 [0.429, 1.437]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 9				
n (%)	44 (62.9)	39 (55.7)	35 (48.6)	33 (45.8)
Mean	57.4	4.9	50.7	-1.2
SD	9.18	5.57	11.39	5.67
Median	61.0	3.0	51.0	0.0
Min, Max	25, 65	-5, 19	21, 65	-19, 11
LS Mean [2]		4.109		-0.696
LS SE [2]		0.7781		0.7826
95% CI [2]		2.569, 5.649		-2.244, 0.852
LS Mean Diff. to Placebo [2]		4.805		
LS SE Diff. to Placebo [2]		1.0457		
95% CI [2]		2.734, 6.876		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.02 [0.530, 1.516]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 10				
n (%)	39 (55.7)	36 (51.4)	28 (38.9)	26 (36.1)
Mean	58.0	5.0	49.4	-1.7
SD	9.30	5.75	11.37	5.25
Median	61.0	3.5	51.5	-0.5
Min, Max	26, 65	-6, 19	29, 65	-16, 8
LS Mean [2]		4.766		-0.621
LS SE [2]		0.7620		0.7894
95% CI [2]		3.258, 6.275		-2.183, 0.941
LS Mean Diff. to Placebo [2]		5.388		
LS SE Diff. to Placebo [2]		1.0404		
95% CI [2]		3.326, 7.449		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.24 [0.688, 1.787]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 11				
n (%)	35 (50.0)	32 (45.7)	26 (36.1)	26 (36.1)
Mean	57.6	5.4	50.6	-0.4
SD	9.52	6.60	9.68	5.46
Median	61.0	5.0	52.5	0.0
Min, Max	24, 65	-8, 20	33, 65	-12, 11
LS Mean [2]		4.983		-0.314
LS SE [2]		0.7971		0.8205
95% CI [2]		3.405, 6.562		-1.938, 1.309
LS Mean Diff. to Placebo [2]		5.298		
LS SE Diff. to Placebo [2]		1.0885		
95% CI [2]		3.141, 7.454		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.21 [0.650, 1.776]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 12				
n (%)	35 (50.0)	34 (48.6)	24 (33.3)	23 (31.9)
Mean	56.2	5.2	53.0	-0.1
SD	11.33	6.45	11.60	5.56
Median	61.0	4.0	56.5	0.0
Min, Max	22, 65	-8, 20	26, 65	-19, 7
LS Mean [2]		4.061		-0.404
LS SE [2]		0.8523		0.9063
95% CI [2]		2.373, 5.749		-2.197, 1.389
LS Mean Diff. to Placebo [2]		4.465		
LS SE Diff. to Placebo [2]		1.1941		
95% CI [2]		2.099, 6.830		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		0.94 [0.387, 1.501]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 13				
n (%)	35 (50.0)	33 (47.1)	23 (31.9)	21 (29.2)
Mean	56.4	4.2	49.3	-1.4
SD	11.01	6.21	12.08	7.95
Median	60.0	4.0	51.0	0.0
Min, Max	25, 65	-10, 20	27, 65	-18, 13
LS Mean [2]		3.848		-1.074
LS SE [2]		1.0055		1.0883
95% CI [2]		1.854, 5.842		-3.229, 1.081
LS Mean Diff. to Placebo [2]		4.922		
LS SE Diff. to Placebo [2]		1.4406		
95% CI [2]		2.065, 7.779		
One-sided p-value [2]		0.0005		
Hedge's G (95% CI)		0.90 [0.324, 1.470]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
PF13 Score				
Cycle 14				
n (%)	34 (48.6)	31 (44.3)	22 (30.6)	20 (27.8)
Mean	58.1	4.9	50.5	0.3
SD	9.39	6.13	12.06	5.98
Median	61.0	4.0	50.5	0.0
Min, Max	26, 65	-7, 20	25, 65	-20, 10
LS Mean [2]		3.953		-0.554
LS SE [2]		0.8908		0.9709
95% CI [2]		2.187, 5.720		-2.478, 1.369
LS Mean Diff. to Placebo [2]		4.507		
LS SE Diff. to Placebo [2]		1.2716		
95% CI [2]		1.985, 7.030		
One-sided p-value [2]		0.0003		
Hedge's G (95% CI)		0.95 [0.361, 1.545]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 15				
n (%)	31 (44.3)	29 (41.4)	23 (31.9)	22 (30.6)
Mean	56.3	5.8	51.8	1.2
SD	10.09	6.07	11.34	5.63
Median	59.0	7.0	57.0	0.0
Min, Max	31, 65	-6, 21	29, 65	-10, 15
LS Mean [2]		4.680		0.769
LS SE [2]		0.8302		0.8852
95% CI [2]		3.035, 6.325		-0.983, 2.521
LS Mean Diff. to Placebo [2]		3.911		
LS SE Diff. to Placebo [2]		1.1594		
95% CI [2]		1.612, 6.210		
One-sided p-value [2]		0.0005		
Hedge's G (95% CI)		0.90 [0.321, 1.483]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 16				
n (%)	35 (50.0)	32 (45.7)	21 (29.2)	19 (26.4)
Mean	57.7	5.7	52.0	0.7
SD	8.76	5.75	11.23	4.99
Median	60.0	5.5	56.0	0.0
Min, Max	28, 65	-6, 20	30, 65	-9, 11
LS Mean [2]		4.818		0.487
LS SE [2]		0.8014		0.8890
95% CI [2]		3.229, 6.407		-1.274, 2.248
LS Mean Diff. to Placebo [2]		4.331		
LS SE Diff. to Placebo [2]		1.1452		
95% CI [2]		2.059, 6.602		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		1.01 [0.406, 1.607]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 17				
n (%)	32 (45.7)	30 (42.9)	21 (29.2)	19 (26.4)
Mean	56.4	5.3	54.6	-0.8
SD	10.87	6.57	10.74	5.11
Median	60.0	4.0	59.0	0.0
Min, Max	25, 65	-8, 19	33, 65	-12, 10
LS Mean [2]		4.678		0.307
LS SE [2]		0.8198		0.9114
95% CI [2]		3.054, 6.302		-1.496, 2.111
LS Mean Diff. to Placebo [2]		4.370		
LS SE Diff. to Placebo [2]		1.1749		
95% CI [2]		2.043, 6.698		
One-sided p-value [2]		0.0002		
Hedge's G (95% CI)		1.00 [0.392, 1.608]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 18				
n (%)	35 (50.0)	33 (47.1)	21 (29.2)	21 (29.2)
Mean	57.1	5.7	53.1	-1.0
SD	9.56	5.63	10.48	4.53
Median	61.0	6.0	56.0	0.0
Min, Max	27, 65	-4, 20	31, 65	-9, 9
LS Mean [2]		4.956		0.028
LS SE [2]		0.7570		0.8412
95% CI [2]		3.457, 6.456		-1.636, 1.692
LS Mean Diff. to Placebo [2]		4.928		
LS SE Diff. to Placebo [2]		1.0757		
95% CI [2]		2.797, 7.060		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.18 [0.592, 1.774]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 19				
n (%)	34 (48.6)	31 (44.3)	21 (29.2)	19 (26.4)
Mean	58.9	6.2	54.6	0.8
SD	6.69	5.90	9.73	5.20
Median	60.0	7.0	55.0	0.0
Min, Max	42, 65	-4, 18	33, 65	-10, 13
LS Mean [2]		5.058		0.454
LS SE [2]		0.7094		0.8083
95% CI [2]		3.653, 6.463		-1.145, 2.053
LS Mean Diff. to Placebo [2]		4.604		
LS SE Diff. to Placebo [2]		1.0151		
95% CI [2]		2.593, 6.615		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.21 [0.594, 1.832]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 20				
n (%)	30 (42.9)	29 (41.4)	16 (22.2)	14 (19.4)
Mean	56.4	5.1	54.6	1.2
SD	10.53	6.05	9.97	4.21
Median	59.0	5.0	56.5	0.0
Min, Max	29, 65	-7, 20	31, 65	-3, 13
LS Mean [2]		3.821		0.417
LS SE [2]		0.8546		1.0377
95% CI [2]		2.125, 5.517		-1.640, 2.475
LS Mean Diff. to Placebo [2]		3.404		
LS SE Diff. to Placebo [2]		1.2966		
95% CI [2]		0.829, 5.978		
One-sided p-value [2]		0.0051		
Hedge's G (95% CI)		0.76 [0.104, 1.419]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
PF13 Score				
Cycle 21				
n (%)	32 (45.7)	31 (44.3)	15 (20.8)	14 (19.4)
Mean	57.3	5.6	53.6	0.9
SD	8.95	5.67	9.49	4.62
Median	60.0	6.0	54.0	0.0
Min, Max	36, 65	-5, 20	35, 65	-3, 15
LS Mean [2]		4.552		0.108
LS SE [2]		0.7181		0.8836
95% CI [2]		3.129, 5.975		-1.641, 1.857
LS Mean Diff. to Placebo [2]		4.444		
LS SE Diff. to Placebo [2]		1.0846		
95% CI [2]		2.294, 6.593		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.15 [0.474, 1.822]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 22				
n (%)	31 (44.3)	29 (41.4)	20 (27.8)	18 (25.0)
Mean	57.1	5.7	55.7	2.5
SD	9.55	6.64	8.77	5.51
Median	60.0	7.0	57.0	0.5
Min, Max	32, 65	-9, 18	33, 65	-5, 19
LS Mean [2]		4.628		1.288
LS SE [2]		0.7851		0.9268
95% CI [2]		3.072, 6.184		-0.547, 3.124
LS Mean Diff. to Placebo [2]		3.340		
LS SE Diff. to Placebo [2]		1.1671		
95% CI [2]		1.026, 5.654		
One-sided p-value [2]		0.0025		
Hedge's G (95% CI)		0.80 [0.187, 1.407]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 23				
n (%)	29 (41.4)	28 (40.0)	14 (19.4)	12 (16.7)
Mean	56.1	5.1	53.8	-0.2
SD	9.35	5.99	10.73	3.07
Median	59.0	5.5	56.0	0.0
Min, Max	35, 65	-7, 19	31, 65	-7, 5
LS Mean [2]		5.013		-0.158
LS SE [2]		0.7568		0.9665
95% CI [2]		3.510, 6.516		-2.076, 1.760
LS Mean Diff. to Placebo [2]		5.171		
LS SE Diff. to Placebo [2]		1.1800		
95% CI [2]		2.826, 7.516		
One-sided p-value [2]		<0.0001		
Hedge's G (95% CI)		1.32 [0.589, 2.061]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 24				
n (%)	22 (31.4)	20 (28.6)	11 (15.3)	9 (12.5)
Mean	59.7	7.2	52.1	-1.4
SD	7.49	5.09	12.37	3.64
Median	63.0	7.0	58.0	-2.0
Min, Max	40, 65	0, 19	27, 65	-7, 6
Cycle 25				
n (%)	19 (27.1)	17 (24.3)	5 (6.9)	4 (5.6)
Mean	60.2	6.2	43.6	-3.3
SD	6.93	6.11	14.38	4.50
Median	64.0	5.0	41.0	-3.0
Min, Max	40, 65	-3, 21	25, 59	-9, 2

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 26				
n (%)	12 (17.1)	9 (12.9)	6 (8.3)	6 (8.3)
Mean	59.8	7.0	48.7	0.5
SD	6.42	8.51	15.11	4.28
Median	61.0	6.0	49.0	2.0
Min, Max	42, 65	-7, 20	26, 64	-8, 4
Cycle 27				
n (%)	12 (17.1)	9 (12.9)	4 (5.6)	4 (5.6)
Mean	56.8	5.0	49.3	1.0
SD	10.01	6.69	13.67	3.56
Median	58.0	5.0	48.5	0.0
Min, Max	31, 65	-7, 17	37, 63	-2, 6

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 28				
n (%)	12 (17.1)	10 (14.3)	3 (4.2)	3 (4.2)
Mean	58.2	6.1	52.0	-2.3
SD	8.44	7.34	14.00	2.08
Median	61.5	6.5	58.0	-3.0
Min, Max	41, 65	-4, 21	36, 62	-4, 0
Cycle 29				
n (%)	12 (17.1)	11 (15.7)	3 (4.2)	3 (4.2)
Mean	55.3	6.1	51.0	-0.3
SD	7.35	7.16	10.39	4.51
Median	56.5	7.0	57.0	0.0
Min, Max	42, 65	-6, 19	39, 57	-5, 4

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 30				
n (%)	8 (11.4)	8 (11.4)	4 (5.6)	4 (5.6)
Mean	56.8	8.8	49.8	5.0
SD	7.83	5.78	12.69	12.57
Median	59.0	9.0	54.5	3.0
Min, Max	40, 65	1, 20	31, 59	-8, 22
Cycle 31				
n (%)	7 (10.0)	7 (10.0)	5 (6.9)	5 (6.9)
Mean	58.1	7.3	53.0	3.0
SD	6.12	8.44	10.42	9.43
Median	60.0	6.0	56.0	0.0
Min, Max	46, 65	-4, 19	35, 62	-5, 18

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 32				
n (%)	6 (8.6)	6 (8.6)	2 (2.8)	2 (2.8)
Mean	56.3	8.8	59.5	-2.5
SD	6.25	8.93	2.12	2.12
Median	58.0	8.5	59.5	-2.5
Min, Max	45, 62	-4, 21	58, 61	-4, -1
Cycle 33				
n (%)	5 (7.1)	5 (7.1)	0	0
Mean	57.4	9.6		
SD	8.91	8.47		
Median	60.0	11.0		
Min, Max	42, 65	-4, 19		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 34				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	65.0	11.0		
SD	NA	NA		
Median	65.0	11.0		
Min, Max	65, 65	11, 11		
Cycle 36				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	65.0	7.0		
SD	NA	NA		
Median	65.0	7.0		
Min, Max	65, 65	7, 7		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
PF13 Score				
Cycle 37				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	65.0	7.0		
SD	NA	NA		
Median	65.0	7.0		
Min, Max	65, 65	7, 7		
Cycle 40				
n (%)	1 (1.4)	1 (1.4)	0	0
Mean	44.0	8.0		
SD	NA	NA		
Median	44.0	8.0		
Min, Max	44, 44	8, 8		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

Table 64.5.1
Summary and Change from Baseline in PROMIS PF Scores by Visit - Double-Blind Phase
PF10A T-Score, PF13 Sum Score
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
PF13 Score				
Follow-Up				
n (%)	7 (10.0)	7 (10.0)	1 (1.4)	0 (0.0)
Mean	55.9	2.9	58.0	
SD	9.75	4.74	NA	
Median	59.0	2.0	58.0	
Min, Max	40, 65	-3, 12	58, 58	

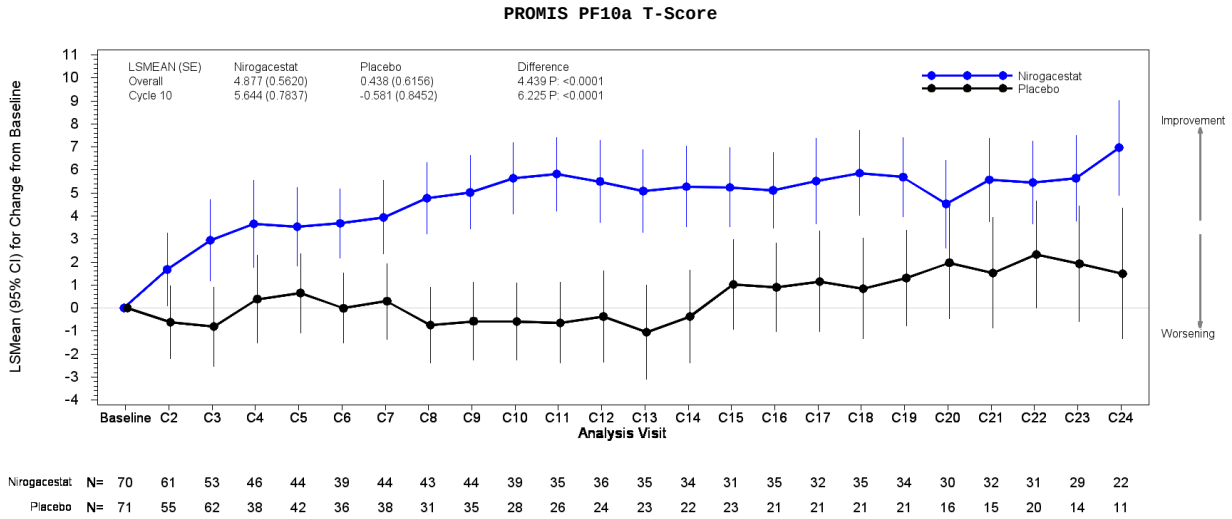
Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
CI = Confidence interval; LS = Least squares; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; SE = Standard error
Note: A positive change from Baseline value indicated improvement of symptoms and a negative change from Baseline value indicated worsening of symptoms. A positive LS mean difference (between Nirogacestat and placebo) favored Nirogacestat over placebo.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] LS mean, LS mean differences, SE and p-values were from a mixed model with repeated measures (MMRM) with treatment and visit as factors, corresponding Baseline PROMIS PF score and primary tumor location (intra-abdominal or extra-abdominal) as covariates, and included Baseline by visit and treatment by visit interactions. A heterogenous Toeplitz (PROMIS 13) or a heterogenous autoregressive 1 (PROMIS T-score) covariance structure was used and degrees of freedom were estimated using the Kenward-Roger approximation.
Only participants with a Baseline and at least one post-Baseline score were included in the analysis. Scheduled visits with at least 10 participants in each arm were included in the model.

Program Name: t_sum_pro.sas Output Generated: 2025-05-21T11:56 Source: ADSL, ADQS

1.7.2 Figure MMRM PROMIS PF

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2025_GBA

Figure 64.5.2
Mixed Model Repeated Measures: Change from Baseline in PROMIS PF Scores by Visit - Double Blind Phase
Intent-to-Treat Population



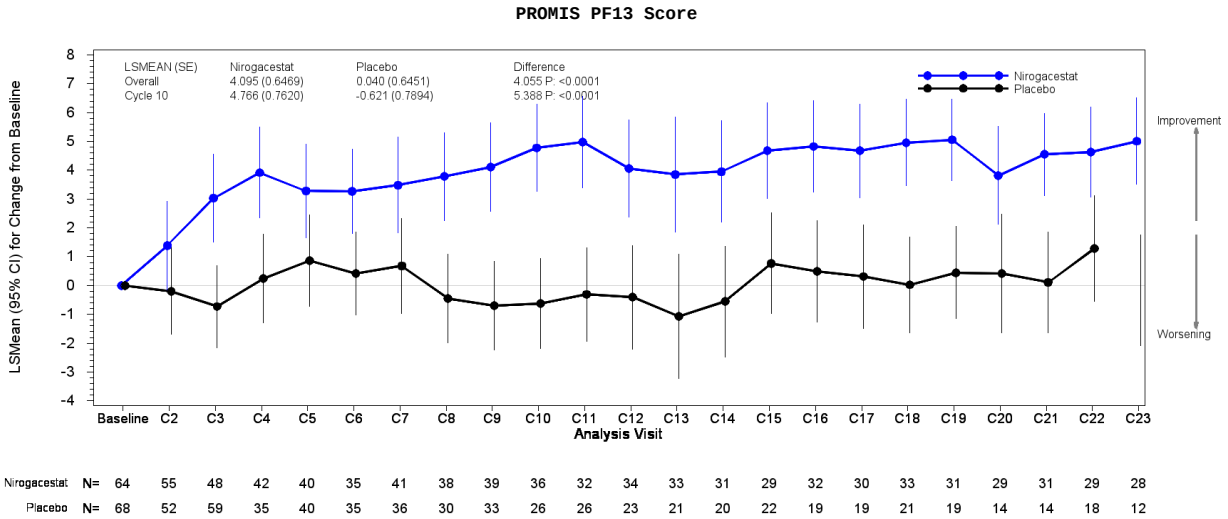
Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.5.1, Dataset(s): ADSL, ADQS

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2025_GBA

Figure 64.5.2
Mixed Model Repeated Measures: Change from Baseline in PROMIS PF Scores by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.5.1, Dataset(s): ADSL, ADQS

1.8 Tumor volume

1.8.1 Table MMRM tumor volume

SpringWorks Therapeutics NIR-DT-301
2025_GBA

Table 64.8.1
Summary and Change from Baseline in Tumor Volume (mL) Assessed by MRI by Visit - Double Blind Phase
Largest Target Lesion Per Participant
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Tumor Volume (mL)				
Baseline [1]				
n (%)	67 (95.7)		70 (97.2)	
Mean	421.166		371.999	
SD	764.6960		519.5409	
Median	151.980		162.385	
Min, Max	4.67, 4912.85		1.95, 2601.39	
Effect over Study Duration				
n (%)		56 (80.0)		57 (79.2)
LS Mean [2]		-216.631		-40.087
LS SE [2]		32.9702		38.6832
95% CI [2]		-281.902, -151.360		-116.441, 36.267
LS Mean Diff. to Placebo [2]		-176.544		
LS SE Diff. to Placebo [2]		47.5794		
95% CI [2]		-270.533, -82.556		
One-sided p-value [2]		0.0001		
Hedge's G (95% CI)		-0.65 [-1.031, -0.274]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
Note: Volume assessments were performed using MRI every 6 cycles.
Note: Volume assessments were performed only on the largest tumor at Baseline.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] Least Square (LS) mean, LS mean differences, standard errors (SE) and p-values were from a mixed model with repeated measures (MMRM) with treatment, Baseline volume, visit, primary tumor location (intra-abdominal or extra-abdominal) and treatment-by-visit interaction as covariates. An autoregressive 1 covariance structure was used, and degrees of freedom were estimated using the Kenward-Roger approximation.

Program Name: t_sum_tvol.sas Output Generated: 2025-05-21T12:33 Source: ADSL, ADTR

Table 64.8.1
Summary and Change from Baseline in Tumor Volume (mL) Assessed by MRI by Visit - Double Blind Phase
Largest Target Lesion Per Participant
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Tumor Volume (mL)				
Cycle 7 Day 1				
n (%)	55 (78.6)	55 (78.6)	55 (76.4)	54 (75.0)
Mean	302.331	-73.917	308.621	47.953
SD	423.0720	285.4646	340.0663	155.6049
Median	133.640	-15.830	196.240	20.020
Min, Max	0.72, 1830.41	-1072.54, 492.91	0.24, 1366.82	-553.58, 466.12
LS Mean [2]		-108.357		-28.155
LS SE [2]		34.4405		34.5701
95% CI [2]		-176.420, -40.295		-96.470, 40.161
LS Mean Diff. to Placebo [2]		-80.203		
LS SE Diff. to Placebo [2]		45.9301		
95% CI [2]		-170.936, 10.531		
One-sided p-value [2]		0.0414		
Hedge's G (95% CI)		-0.31 [-0.693, 0.063]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
Note: Volume assessments were performed using MRI every 6 cycles.
Note: Volume assessments were performed only on the largest tumor at Baseline.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] Least Square (LS) mean, LS mean differences, standard errors (SE) and p-values were from a mixed model with repeated measures (MMRM) with treatment, Baseline volume, visit, primary tumor location (intra-abdominal or extra-abdominal) and treatment-by-visit interaction as covariates. An autoregressive 1 covariance structure was used, and degrees of freedom were estimated using the Kenward-Roger approximation.

Program Name: t_sum_tvol.sas Output Generated: 2025-05-21T12:33 Source: ADSL, ADTR

Table 64.8.1
Summary and Change from Baseline in Tumor Volume (mL) Assessed by MRI by Visit - Double Blind Phase
Largest Target Lesion Per Participant
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Tumor Volume (mL)				
Cycle 13 Day 1				
n (%)	47 (67.1)	47 (67.1)	37 (51.4)	37 (51.4)
Mean	208.831	-181.684	294.410	6.209
SD	351.9064	405.7896	364.4708	219.6532
Median	63.500	-52.800	134.310	24.020
Min, Max	0, 1434.95	-1831.08, 319.64	0.10, 1160.56	-752.19, 476.78
LS Mean [2]		-190.285		-41.808
LS SE [2]		35.2019		36.8809
95% CI [2]		-259.812, -120.758		-114.583, 30.966
LS Mean Diff. to Placebo [2]		-148.477		
LS SE Diff. to Placebo [2]		48.1649		
95% CI [2]		-243.523, -53.431		
One-sided p-value [2]		0.0012		
Hedge's G (95% CI)		-0.63 [-1.076, -0.193]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
Note: Volume assessments were performed using MRI every 6 cycles.
Note: Volume assessments were performed only on the largest tumor at Baseline.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] Least Square (LS) mean, LS mean differences, standard errors (SE) and p-values were from a mixed model with repeated measures (MMRM) with treatment, Baseline volume, visit, primary tumor location (intra-abdominal or extra-abdominal) and treatment-by-visit interaction as covariates. An autoregressive 1 covariance structure was used, and degrees of freedom were estimated using the Kenward-Roger approximation.

Program Name: t_sum_tvol.sas Output Generated: 2025-05-21T12:33 Source: ADSL, ADTR

Table 64.8.1
Summary and Change from Baseline in Tumor Volume (mL) Assessed by MRI by Visit - Double Blind Phase
Largest Target Lesion Per Participant
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Tumor Volume (mL)				
Cycle 19 Day 1				
n (%)	43 (61.4)	43 (61.4)	25 (34.7)	25 (34.7)
Mean	196.136	-228.518	247.246	-17.707
SD	321.0547	440.2355	338.1528	333.7224
Median	43.760	-69.420	109.210	1.150
Min, Max	0, 1100.15	-1911.31, 369.11	0.73, 1099.99	-825.74, 932.31
LS Mean [2]		-221.179		-40.582
LS SE [2]		36.1412		41.3083
95% CI [2]		-292.528, -149.830		-121.978, 40.814
LS Mean Diff. to Placebo [2]		-180.597		
LS SE Diff. to Placebo [2]		52.3246		
95% CI [2]		-283.736, -77.458		
One-sided p-value [2]		0.0003		
Hedge's G (95% CI)		-0.80 [-1.309, -0.287]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
Note: Volume assessments were performed using MRI every 6 cycles.
Note: Volume assessments were performed only on the largest tumor at Baseline.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] Least Square (LS) mean, LS mean differences, standard errors (SE) and p-values were from a mixed model with repeated measures (MMRM) with treatment, Baseline volume, visit, primary tumor location (intra-abdominal or extra-abdominal) and treatment-by-visit interaction as covariates. An autoregressive 1 covariance structure was used, and degrees of freedom were estimated using the Kenward-Roger approximation.

Program Name: t_sum_tvol.sas Output Generated: 2025-05-21T12:33 Source: ADSL, ADTR

Table 64.8.1
Summary and Change from Baseline in Tumor Volume (mL) Assessed by MRI by Visit - Double Blind Phase
Largest Target Lesion Per Participant
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	Nirogacestat (N=70) Change from Baseline	Placebo (N=72) Actual Value	Placebo (N=72) Change from Baseline
Tumor Volume (mL)				
Cycle 25 Day 1				
n (%)	23 (32.9)	23 (32.9)	8 (11.1)	8 (11.1)
Mean	165.323	-266.146	196.811	-73.176
SD	271.1504	536.5652	329.9111	336.5208
Median	23.580	-56.950	89.770	-12.250
Min, Max	0, 1067.05	-2261.11, 371.16	2.92, 996.65	-864.26, 281.06
LS Mean [2]		-270.877		-47.523
LS SE [2]		41.3245		57.8563
95% CI [2]		-352.301, -189.454		-161.372, 66.326
LS Mean Diff. to Placebo [2]		-223.354		
LS SE Diff. to Placebo [2]		69.1638		
95% CI [2]		-359.464, -87.245		
One-sided p-value [2]		0.0007		
Hedge's G (95% CI)		-1.14 [-1.996, -0.289]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
Note: Volume assessments were performed using MRI every 6 cycles.
Note: Volume assessments were performed only on the largest tumor at Baseline.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] Least Square (LS) mean, LS mean differences, standard errors (SE) and p-values were from a mixed model with repeated measures (MMRM) with treatment, Baseline volume, visit, primary tumor location (intra-abdominal or extra-abdominal) and treatment-by-visit interaction as covariates. An autoregressive 1 covariance structure was used, and degrees of freedom were estimated using the Kenward-Roger approximation.

Program Name: t_sum_tvol.sas Output Generated: 2025-05-21T12:33 Source: ADSL, ADTR

Table 64.8.1
Summary and Change from Baseline in Tumor Volume (mL) Assessed by MRI by Visit - Double Blind Phase
Largest Target Lesion Per Participant
Intent-to-Treat Population

Score Timepoint	Nirogacestat (N=70) Actual Value	 Change from Baseline	Placebo (N=72) Actual Value	 Change from Baseline
Tumor Volume (mL)				
Cycle 31 Day 1				
n (%)	11 (15.7)	11 (15.7)	4 (5.6)	4 (5.6)
Mean	107.861	-404.274	391.140	34.040
SD	185.2820	748.7479	396.0316	155.7851
Median	11.130	-57.800	347.935	-5.705
Min, Max	0.92, 501.00	-2382.26, -1.71	31.41, 837.28	-104.65, 252.22
LS Mean [2]		-304.698		-119.042
LS SE [2]		53.6597		83.9473
95% CI [2]		-410.302, -199.093		-284.243, 46.160
LS Mean Diff. to Placebo [2]		-185.656		
LS SE Diff. to Placebo [2]		98.3606		
95% CI [2]		-379.213, 7.901		
One-sided p-value [2]		0.0300		
Hedge's G (95% CI)		-0.99 [-2.193, 0.204]		

Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
Note: Volume assessments were performed using MRI every 6 cycles.
Note: Volume assessments were performed only on the largest tumor at Baseline.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] Least Square (LS) mean, LS mean differences, standard errors (SE) and p-values were from a mixed model with repeated measures (MMRM) with treatment, Baseline volume, visit, primary tumor location (intra-abdominal or extra-abdominal) and treatment-by-visit interaction as covariates. An autoregressive 1 covariance structure was used, and degrees of freedom were estimated using the Kenward-Roger approximation.

Program Name: t_sum_tvol.sas Output Generated: 2025-05-21T12:33 Source: ADSL, ADTR

Table 64.8.1
Summary and Change from Baseline in Tumor Volume (mL) Assessed by MRI by Visit - Double Blind Phase
Largest Target Lesion Per Participant
Intent-to-Treat Population

	Nirogacestat (N=70)		Placebo (N=72)	
Score Timepoint	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Tumor Volume (mL)				
End of Treatment				
n (%)	7 (10.0)	7 (10.0)	5 (6.9)	5 (6.9)
Mean	102.430	-74.403	714.444	-71.570
SD	136.2755	124.1023	969.8587	464.3401
Median	21.100	-49.500	351.340	84.310
Min, Max	0, 297.72	-311.56, 75.70	45.31, 2427.49	-895.80, 196.66
LS Mean [2]		-204.392		36.587
LS SE [2]		78.1372		102.5863
95% CI [2]		-358.175, -50.608		-165.503, 238.677
LS Mean Diff. to Placebo [2]		-240.979		
LS SE Diff. to Placebo [2]		127.2182		
95% CI [2]		-491.460, 9.502		
One-sided p-value [2]		0.0296		
Hedge's G (95% CI)		-1.03 [-2.249, 0.190]		

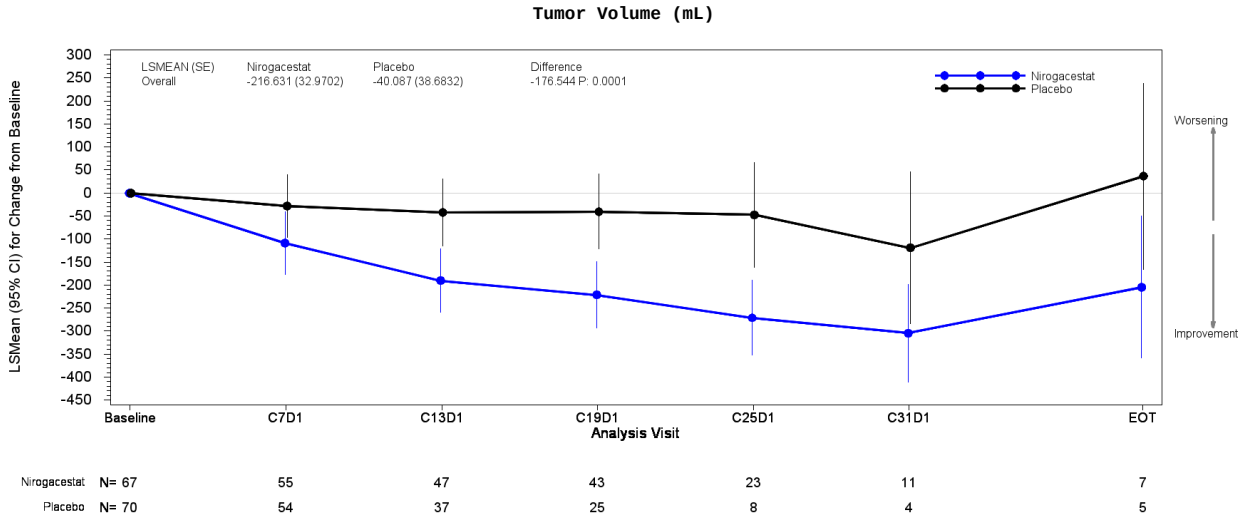
Database Lock: 17-May-2022, Data Cutoff: 07-Apr-2022
Note: Volume assessments were performed using MRI every 6 cycles.
Note: Volume assessments were performed only on the largest tumor at Baseline.
[1] Baseline was defined as the most recent measurement prior to the first administration of study treatment.
[2] Least Square (LS) mean, LS mean differences, standard errors (SE) and p-values were from a mixed model with repeated measures (MMRM) with treatment, Baseline volume, visit, primary tumor location (intra-abdominal or extra-abdominal) and treatment-by-visit interaction as covariates. An autoregressive 1 covariance structure was used, and degrees of freedom were estimated using the Kenward-Roger approximation.

Program Name: t_sum_tvol.sas Output Generated: 2025-05-21T12:33 Source: ADSL, ADTR

1.8.2 Figure MMRM tumor volume

SpringWorks Therapeutics
NIR-DT-301
2025_GBA

Figure 64.8.2
Mixed Model Repeated Measures: Change from Baseline in Tumor Volume (mL) Assessed by MRI by Visit - Double Blind Phase
Intent-to-Treat Population



Database Lock: 17-May-2022 , Data Cutoff: 07-Apr-2022

Program Name: f_pro.sas, Output Generated: 2025-05-21T12:38, Source: Table 64.8.1, Dataset(s): ADSL, ADTR

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2 Prädefinierte MCID

2.1 BPI worst pain

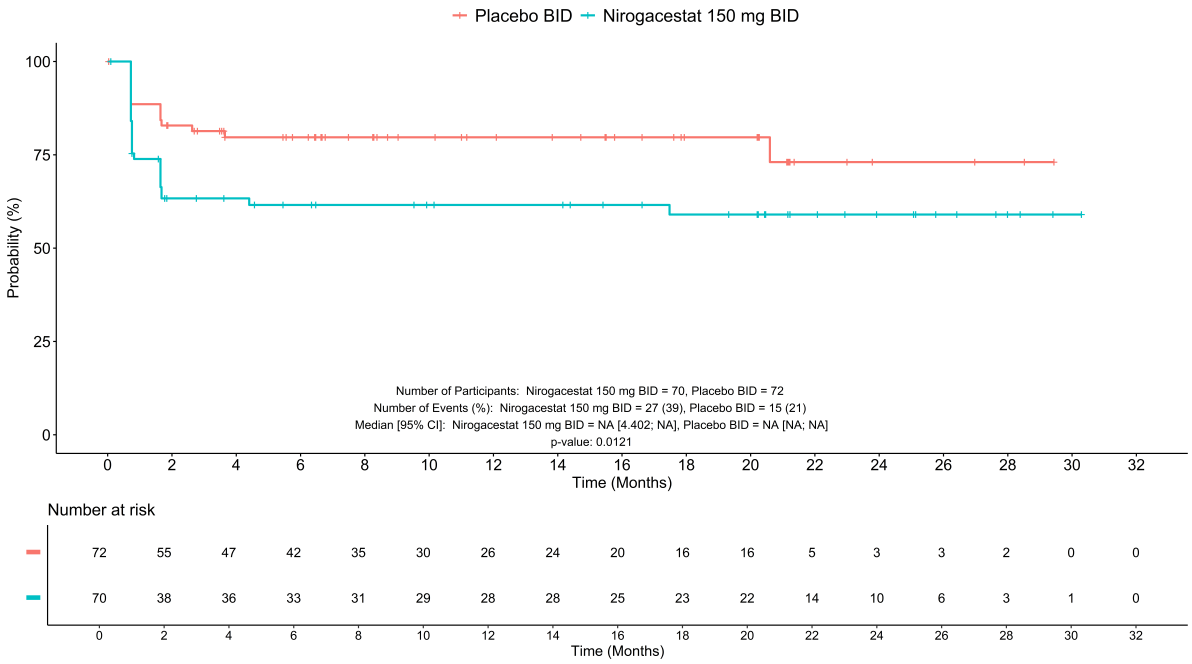
2.1.1 Improvement of 2 points BPI-worst pain

2.1.1.1 PRBPI ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	27 (39)	15 (21)
min_max_months	[0.10 ,30.29]	[0.03 ,29.44]
10 percentile	0.72	0.72
25 percentile	0.82	20.60
50 percentile	NA [4.402; NA]	NA [NA; NA]
75 percentile	NA	NA
90 percentile	NA	NA

	Value
PH_test_p	0.8149
HR	2.10
HR_95_CI	[1.089; 4.054]
HR_p	0.0121

2.1.1.2 PRBPI km



2.2 GODDESS DTIS

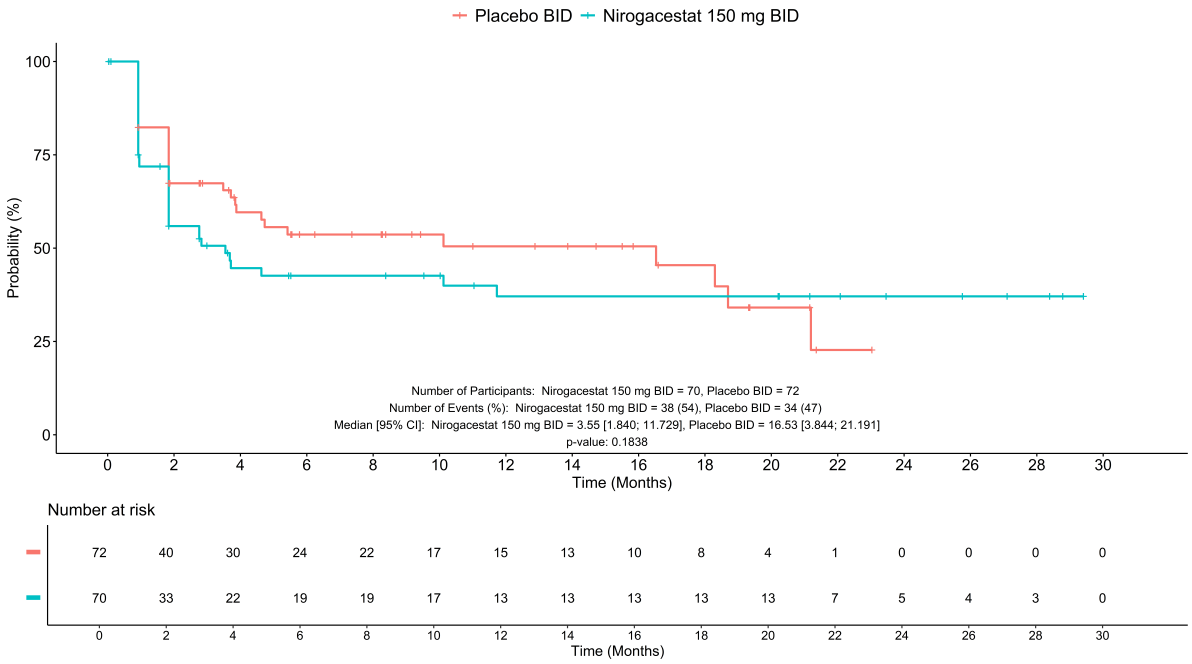
2.2.1 Domänenscore Emotion-Verbesserung um ≥ 1,7 Punkte

2.2.1.1 IMEMTN ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	38 (54)	34 (47)
min_max_months	[0.03 ,29.40]	[0.03 ,23.03]
10 percentile	0.92	0.92
25 percentile	0.94	1.84
50 percentile	3.55 [1.840; 11.729]	16.53 [3.844; 21.191]
75 percentile	NA	21.19
90 percentile	NA	NA

	Value
PH_test_p	0.1537
HR	1.26
HR_95_CI	[0.763; 2.076]
HR_p	0.1838

2.2.1.2 IMEMTN km



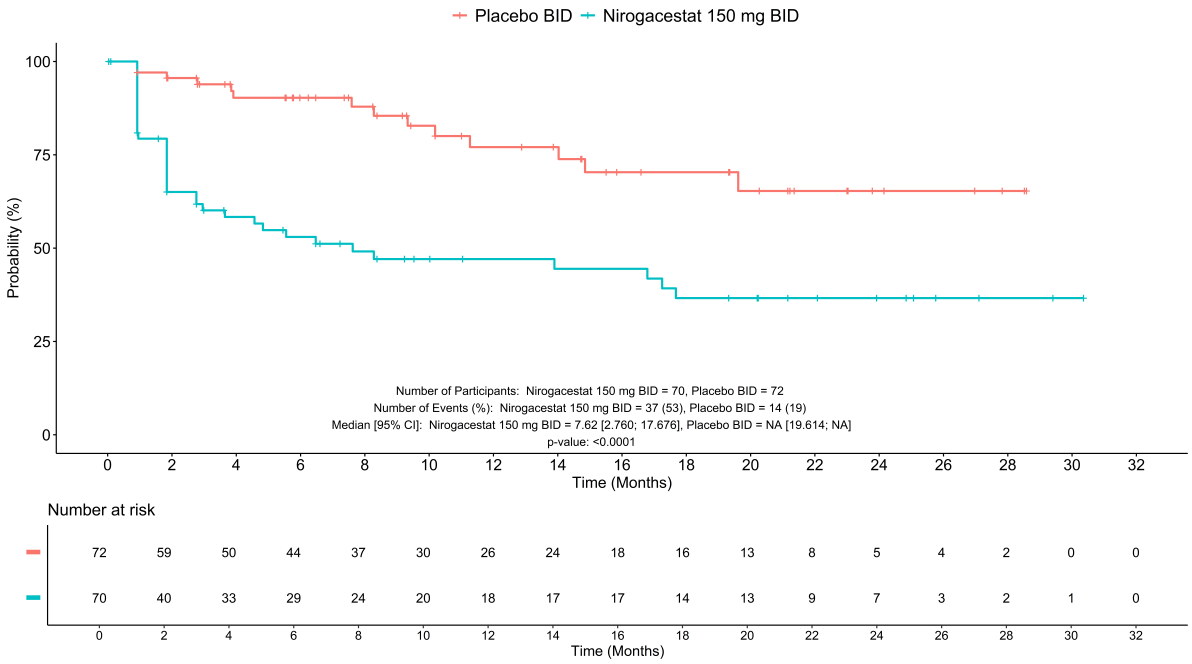
2.2.2 Domänenscore Körperliche Funktion-Verbesserung um ≥ 0,8 Punkte

2.2.2.1 IMPFUN ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	37 (53)	14 (19)
min_max_months	[0.03 ,30.36]	[0.03 ,28.58]
10 percentile	0.92	7.59
25 percentile	1.84	14.03
50 percentile	7.62 [2.760; 17.676]	NA [19.614; NA]
75 percentile	NA	NA
90 percentile	NA	NA

	Value
PH_test_p	0.0210
HR	3.67
HR_95_CI	[1.952; 6.903]
HR_p	<0.0001
rr_MH_est	2.71
rr_MH_95_CI	[1.619; 4.531]
MH_p_val	0.0001

2.2.2.2 IMPFUN km



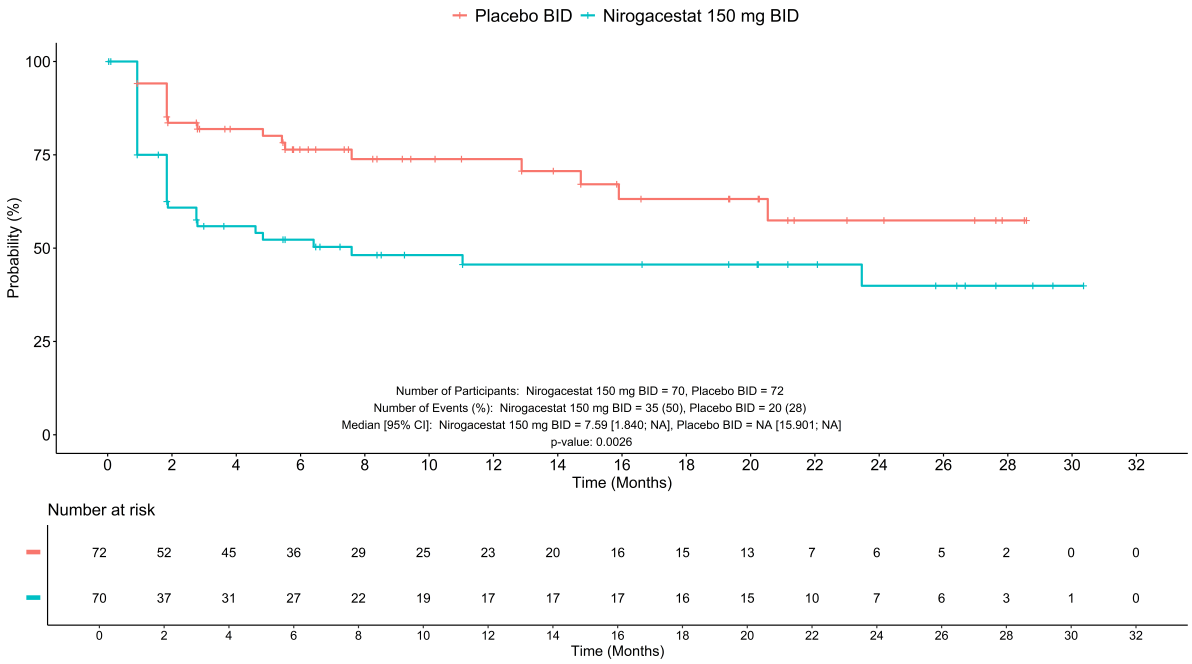
2.2.3 Domänenscore Schlaf-Verbesserung um ≥ 0,7 Punkte

2.2.3.1 IMSLP ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	35 (50)	20 (28)
min_max_months	[0.03 ,30.36]	[0.03 ,28.58]
10 percentile	0.92	1.84
25 percentile	1.38	7.59
50 percentile	7.59 [1.840; NA]	NA [15.901; NA]
75 percentile	NA	NA
90 percentile	NA	NA

	Value
PH_test_p	0.0441
HR	2.24
HR_95_CI	[1.256; 3.978]
HR_p	0.0026
rr_MH_est	1.80
rr_MH_95_CI	[1.157; 2.792]
MH_p_val	0.0091

2.2.3.2 IMSLP km



2.3 GODDESS DTSS

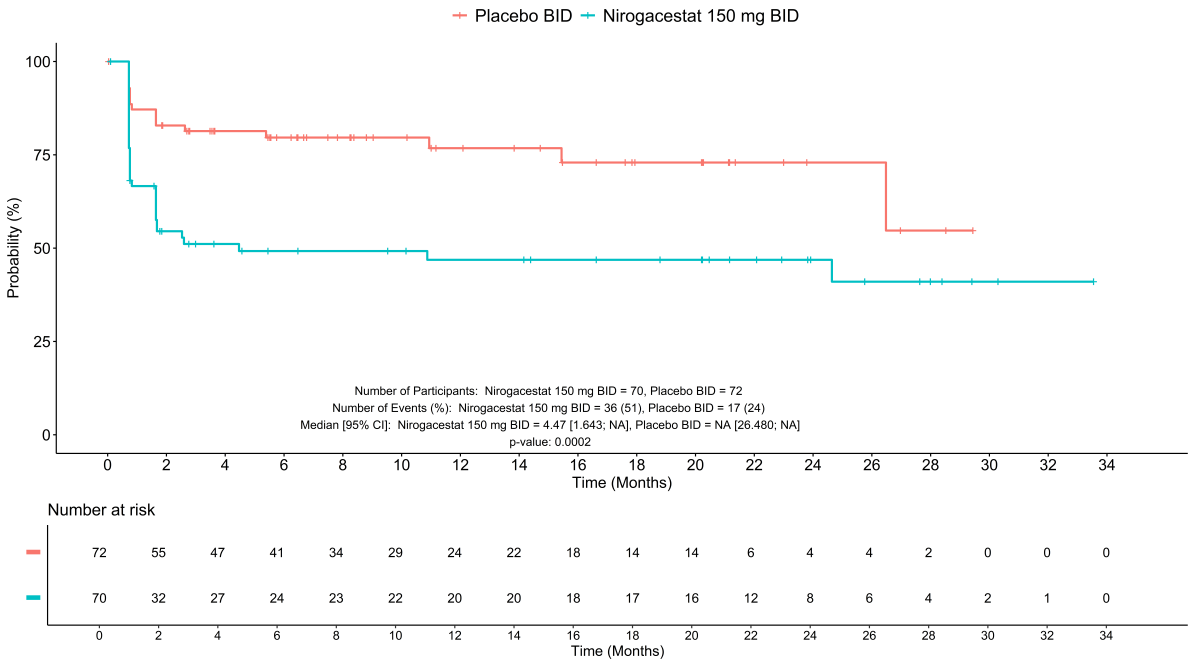
2.3.1 Domänenscore extra-abdominale Symptome-Verbesserung um ≥ 1,9 Punkte

2.3.1.1 PRDTSS ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	36 (51)	17 (24)
min_max_months	[0.10 ,33.54]	[0.03 ,29.44]
10 percentile	0.72	0.76
25 percentile	0.76	15.44
50 percentile	4.47 [1.643; NA]	NA [26.480; NA]
75 percentile	NA	NA
90 percentile	NA	NA

	Value
PH_test_p	0.3635
HR	2.87
HR_95_CI	[1.565; 5.250]
HR_p	0.0002

2.3.1.2 PRDTSS km



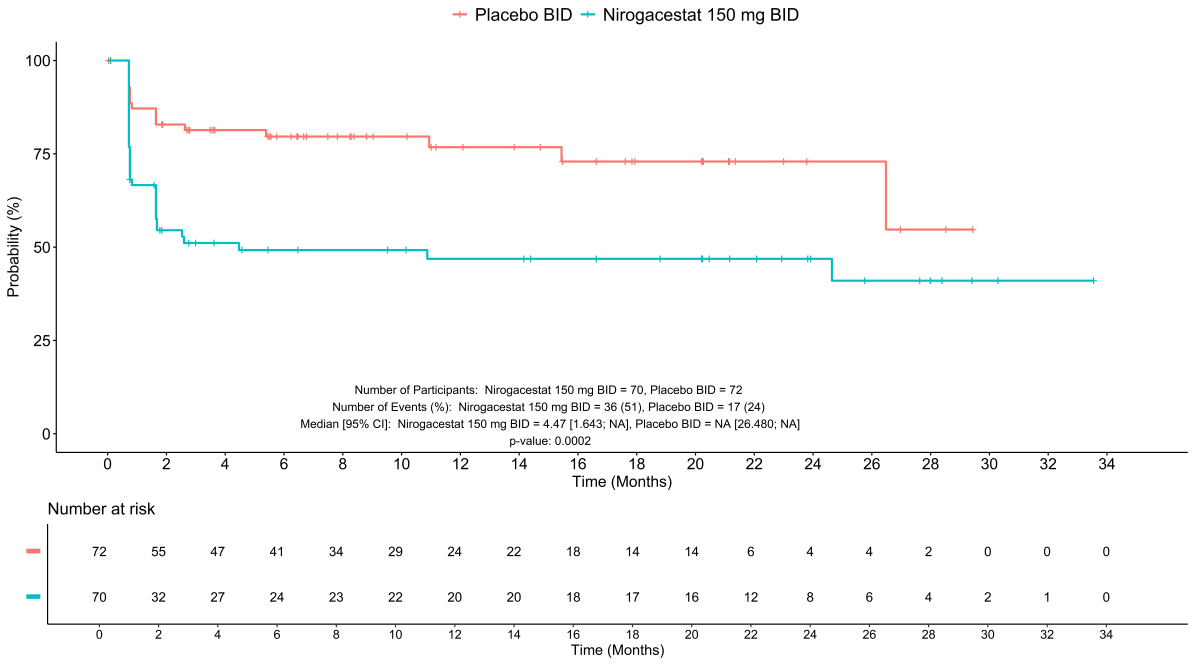
2.3.2 Domänenscore Schmerz-Verbesserung um ≥ 1,9 Punkte

2.3.2.1 PRDTSS ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	36 (51)	17 (24)
min_max_months	[0.10 ,33.54]	[0.03 ,29.44]
10 percentile	0.72	0.76
25 percentile	0.76	15.44
50 percentile	4.47 [1.643; NA]	NA [26.480; NA]
75 percentile	NA	NA
90 percentile	NA	NA

	Value
PH_test_p	0.3635
HR	2.87
HR_95_CI	[1.565; 5.250]
HR_p	0.0002

2.3.2.2 PRDTSS km



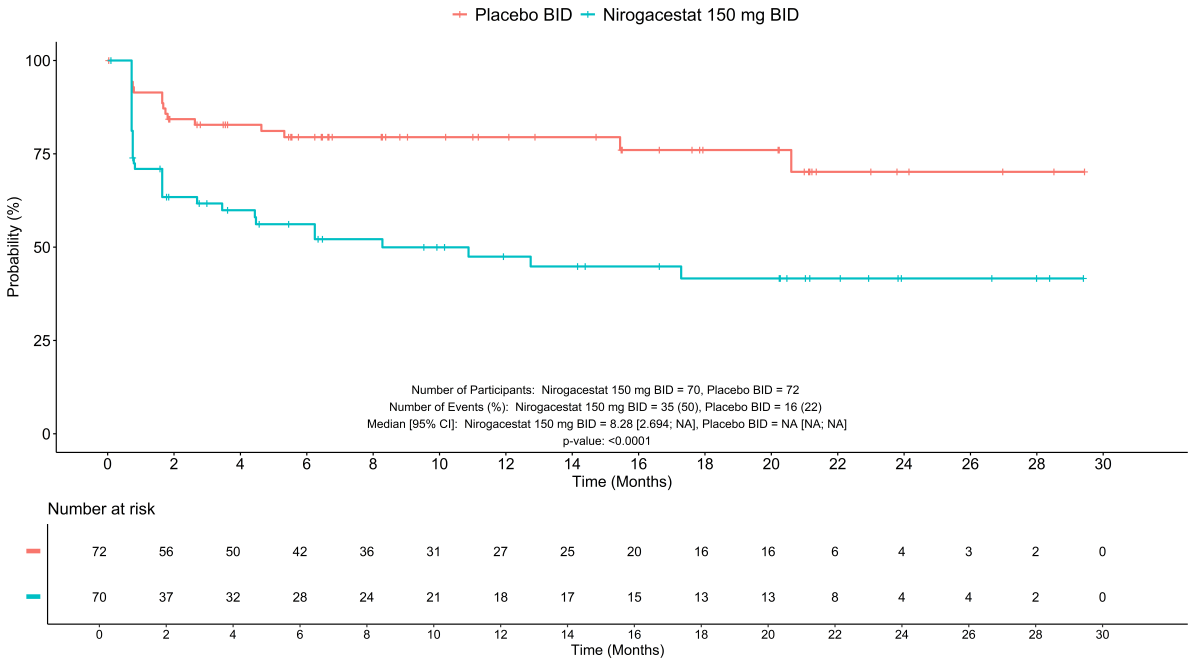
2.3.3 Extra-Abdominal-Domain-Verbesserung um ≥ 1,4 Punkte

2.3.3.1 DTSSEASI ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	35 (50)	16 (22)
min_max_months	[0.10 ,29.40]	[0.03 ,29.44]
10 percentile	0.72	1.64
25 percentile	0.76	20.60
50 percentile	8.28 [2.694; NA]	NA [NA; NA]
75 percentile	NA	NA
90 percentile	NA	NA

	Value
PH_test_p	0.6316
HR	3.06
HR_95_CI	[1.665; 5.615]
HR_p	<0.0001

2.3.3.2 DTSSEASI km



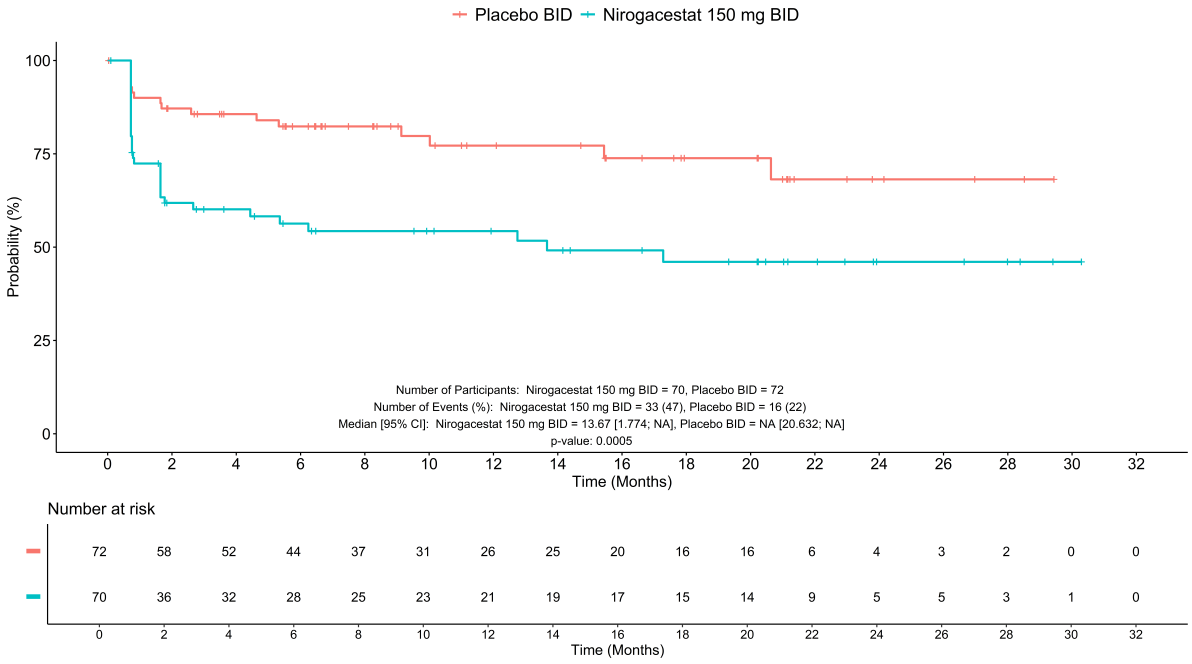
2.3.4 Gesamtscore der Symptome -Verbesserung um ≥ 1,4 Punkte

2.3.4.1 DTSI ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	33 (47)	16 (22)
min_max_months	[0.10 ,30.29]	[0.03 ,29.44]
10 percentile	0.72	1.23
25 percentile	0.79	15.44
50 percentile	13.67 [1.774; NA]	NA [20.632; NA]
75 percentile	NA	NA
90 percentile	NA	NA

	Value
PH_test_p	0.3962
HR	2.72
HR_95_CI	[1.469; 5.038]
HR_p	0.0005

2.3.4.2 DTSI km



2.3.5 Gesamtscore der Symptome-Durchschnitt -Verbesserung um ≥ 1,5 Punkte

2.3.5.1 DTSSAVI ITT

	Nirogacestat 150 mg BID	Placebo BID
N	70	72
n_percent	70(100)	72(100)
Events_percent	34 (49)	17 (24)
min_max_months	[0.10 ,30.29]	[0.03 ,29.44]
10 percentile	0.72	0.74
25 percentile	0.76	15.44
50 percentile	12.75 [1.643; NA]	NA [20.632; NA]
75 percentile	NA	NA
90 percentile	NA	NA

	Value
PH_test_p	0.8923
HR	2.69
HR_95_CI	[1.469; 4.912]
HR_p	0.0005

2.3.5.2 DTSSAVI km

